SCIENCE

AUGUST 1, 1952

VOLUME 116 NUMBER 3005

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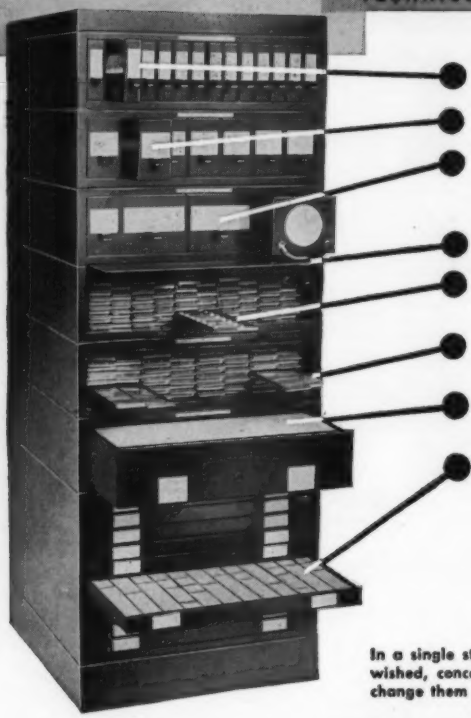

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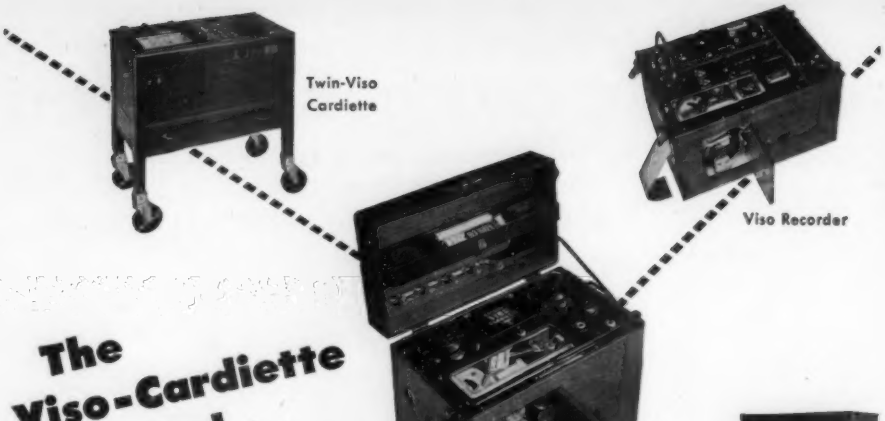

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Solar-Terrestrial Relationships

THE earth, if it were the eighth planet from the sun, would become a barren, frigid mass imbedded with thousands of cubic miles of ice. Terrestrial oceans would be mainly of liquid nitrogen and oxygen, and the atmosphere would consist of a thin, rarefied film of gradually escaping hydrogen and helium.

Luckily, the earth is the third planet of the solar system; its remarkably favorable aspect toward life emphasizes the strong influence of the sun. Earliest man expressed his appreciation of the sun's importance by worship and deification, and a few moments' reflection will reveal that solar-terrestrial relationships are involved, one way or another, in most of man's activities.

Aside from variable fractions of nuclear and tidal power, all available energy resources on the earth stem from solar radiation. The absorbed radiation of past centuries lies locked mainly in fossil carbon, organic remains, and the free oxygen of the atmosphere. Present radiation is stored by photosynthesis, evaporation of water, ionization, and dissociation, but is also available in water-, wind-, and direct solar-power.

The sun, notwithstanding its tremendous importance to earth, is a mediocre star, located near the outskirts of our galaxy and, like so many others, has nothing in the way of size, mass, radiative emission, or other characteristics (with the possible exception of a planetary system) to distinguish it from thousands of others. As it appears today, solar energy results from the thermonuclear fusion of hydrogen into helium, and should last for several billion years. The temperature of the photosphere is roughly taken as 6000° C, but there are indications of emissions at a higher temperature in the ultraviolet region.

The diverse radiations from the sun markedly influence the terrestrial atmosphere. Solar emissions in the x-ray and ultraviolet region of the electromagnetic spectrum produce the ionic layers so important for radio communications. Abnormal radiation in the ultraviolet by solar flares intensifies the lower electrified regions of the terrestrial atmosphere and produces marked, though temporary, changes in the atmospheric parameters. Solar ultraviolet radiation, below 3000 A, penetrates approximately to 20–30 km above the earth's surface, forming the ozone layer, which acts as a life-preserving shield from the otherwise harmful effects of the ultraviolet to mankind below. The remaining radiations, mainly in the visible and infrared, (after partial absorption by the dense, lower atmosphere) reach the earth's surface to warm and sustain life. In general, the net energy influx from the sun must be accounted for; that not stored by one means or another must be reradiated by the earth in order to maintain the temperatures so favorable to life. An important related phase of the study of solar-terrestrial relationships is the weather, particularly the investigation of long-range weather trends—a study yet in its infancy.

The influence of the sun is not limited to fuel reserves and atmospheric influences. Of vital importance is the question of feeding the global population. The greatest single source of usable solar energy (over 99 per cent) occurs through photosynthesis, which is not only the basic source of food but also the greatest source of fuel. Cultivation of vast quantities of algae both for fuel and for food may yet become commonplace, especially after conventional farming methods have been pushed to the limit.

At the Geophysics Research Division many phases of solar-terrestrial relationships are being actively examined. These include studies of the solar spectrum, the solar constant, and the statistical correlation of solar phenomena (such as sunspots, flares, and prominences) with associated terrestrial activity (such as ionospheric disturbances, magnetic variations, aurorae, weather, and variations of atmospheric constituents). The practical applications of the results of this research are innumerable.

R. M. CHAPMAN

Geophysics Research Division
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SCIENCE, founded in 1880, is published each Friday by the American Association for the Advancement of Science at the Business Press, 10 McGovern Ave., Lancaster, Pa. Entered as second-class matter at the Post Office at Lancaster, Pa., January 13, 1948, under the Act of March 3, 1879. Acceptance for mailing at the special rate postage provided for in the Act of February 28, 1925, embodied in Paragraph (d-2) Section 34.40 P. L. & R. of 1948.

All correspondence should be sent to SCIENCE, 1515 Massachusetts Ave., N.W., Washington 5, D. C. The AAAS assumes no responsibility for the safety of manuscripts or for the opinions expressed by contributors. Four weeks' notice is required for change of address, and an address stencil label from a recent issue must be furnished. Claims for a missing number will be allowed only if received within 60 days from date of issue.

Annual subscriptions, $7.50; single copies, $.25; foreign postage, outside the Pan-American Union, $1.00; Canadian postage, $.50. Special rates to members of the AAAS.

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The Constitution and Functions of the United Kingdom Medical Research Council[1]

Francis H. K. Green

Medical Research Council, London, England

I MUST APOLOGIZE for my temerity in coming here, on this, my first visit to the United States, to tell you about a British government organization. I was emboldened to do so by hearing from scientific colleagues who had been lucky enough to visit America earlier than I, and for enviably longer periods, that there is a genuine and widespread interest here in the structure and activities of the U. K. Medical Research Council; and, more decisively, by reading in the issue of SCIENCE of November 16, 1951, the very stimulating article by Leonard A. Scheele and W. H. Sebrell on "Medical Research and Medical Education." I was especially interested, although not much surprised, to find that the U. S. Public Health Service has encountered many of the same problems and difficulties in administering to the best advantage the Congressional funds at its disposal as has the Medical Research Council in administering its Parliamentary grant-in-aid, and that generally similar expedients have been adopted to meet them. It seemed to me, therefore, that you might like to have a factual account of our medical research organization for comparison with your own under the Public Health Service. Later, I hope to refer specifically to some of the analogies between your arrangements and ours, and between our respective methods of dealing with our common problems.

The promotion of medical research in the United Kingdom has been predominantly a government responsibility for nearly 40 years. The funds granted by Parliament to the Medical Research Council for this purpose amount at present to about £1,666,000, or $4,665,000, per annum, exclusive of nonrecurrent provision for capital expenditure on buildings and special equipment, totaling about £232,000, or $650,000, in the current year. In addition to these direct subventions, the government also gives substantial support to medical research—particularly in the basic sciences—through the block grants to universities distributed through the University Grants Committee and—in the clinical field—through the maintenance of hospitals and the payments to doctors under the National Health Service. Thus the major part of U. K. resources for medical research comes directly or indirectly from the national exchequer. Nevertheless, a very important contribution to research in particular subjects is made by private charities, of which the Nuffield Foundation and the British Empire Cancer Campaign are the largest. There is close cooperation between the Medical Research Council and the principal private organizations supporting medical research, with a view to ensuring the most effective allocation of their respective resources and the avoidance of undesirable overlap; it can justly be said, therefore, that medical research is a field in which the philanthropic activities of the state and of private enterprise are successfully coordinated for the public good. It is relevant to remark also that the government organization for medical research—the Medical Research Council—is itself empowered to receive private benefactions to augment the public funds at its disposal; though small in relation to the council's total annual expenditure, these gifts and bequests, usually made for the support of research on particular diseases, provide a welcome supplement to its grants from Parliament.

It may perhaps have come as a surprise to learn that the state provision for medical research in the U. K. is an institution of such respectable antiquity, and not just another manifestation of the increasing intervention of government in human affairs since the end of the second world war. I shall try to explain, as simply as possible, how this came about, and how, from very modest beginnings, the organization has gradually achieved its present magnitude.

When the original National Health Insurance scheme was introduced by Lloyd George in 1911 (to the inevitable cries of public execration and dismay, which I am old enough to remember), provision was made in the act for a sum of money calculated on the basis of one penny for each insured person in the United Kingdom to be set aside annually as a Medical Research Fund. A special Medical Research Committee was appointed to administer the fund, and the late Sir Walter Fletcher, who was to become the first secretary of the Medical Research Council, was persuaded to leave his academic and research post as fellow and senior tutor at Trinity College, Cambridge, to become the committee's secretary. It was significant for the whole course of development of state-aided medical research in Great Britain that the chief executive officer of the Medical Research Committee should

[1] Based on lecture delivered at the National Institutes of Health, U. S. Public Health Service, Bethesda, Md., April 2, 1952.

himself have been not only a medical man but a research scientist of distinction. His work with Gowland Hopkins at Cambridge on lactic acid in muscle had earned him a fellowship of the Royal Society. Even before Fletcher's appointment in the early summer of 1914, the Medical Research Committee had acquired a disused hospital at Hampstead, London, as the building for a National Institute for Medical Research, and had begun to make plans for a research program within the limited funds at its disposal, then amounting to about £55,000 per annum. These plans were rapidly completed under Fletcher's guidance, but they had been only partly implemented when the normal life of the country was disrupted by the impact of the first world war. From the committee's point of view this meant that its program of fundamental researches in pathology, physiology, and biochemistry, and of direct attack on diseases such as tuberculosis and rheumatism, had mostly to be shelved, and it had instead to cooperate with the Army Medical Service in studying problems of more urgent military significance, such as wound infection, shock, and the dysenteries. Study of the committee's reports on work carried out on many different subjects during the war of 1914–18 makes it clear that the committee honorably won its spurs at that time, and there is no doubt that the fact that it did so was largely responsible for its being perpetuated as a separate body when the Ministry of Health was created in 1919.

It might seem logical to have attached the Medical Research Committee to the new ministry. That this was not done was not just another manifestation of British contrariness, for there were cogent reasons against it. I have indicated one reason why the concept of an independent Medical Research Committee was perpetuated. Other reasons, of even greater force, were set forth in a historic memorandum presented to Parliament by Christopher Addison, who was then president of the Local Government Board and became the first minister of health, at the time when the bill to set up the ministry was under discussion. In this it was pointed out that a progressive Ministry of Health must necessarily become deeply committed from time to time to particular policies of health administration and that, if the medical research organization were placed directly under the minister, it might find itself constrained to keep in step with the ministry's current policies, instead of being entirely at liberty to recommend alterations of those policies in the light of new knowledge; its activities, moreover, might tend to be undesirably limited to the study of "those problems which appeared at the moment to be of the most pressing practical importance" from the point of view of the ministry's executive functions, to the exclusion of the more fundamental studies upon which all advances in knowledge of short-term practical problems must ultimately be based, and which of themselves have so often been found to lead suddenly and unexpectedly to new advances in the practice of medicine. Such a myopic view of the functions of medical science could best be avoided by leaving the promotion of medical research in the hands of the relatively autonomous body of scientific experts which had already proved its value, and which should be given (in the words of the memorandum) "the widest possible freedom" to make new discoveries within its field, and to make them available for the use of any or all of the executive government departments, and of the medical profession, without regard to questions of political or administrative expediency. It was realized that the Ministry of Health ought itself to have power to employ a research staff to undertake short-term investigations of practical problems related to its work, and this was given in the act; it may be added, parenthetically, that power to promote medical research is also given to the minister under the Act of 1946, which set up the National Health Service; the relative functions of the Medical Research Council and the ministry in this regard are a matter of amicable arrangements between the council and the ministry.

Another important reason against incorporating the Medical Research Committee in the Ministry of Health, which was adduced in the Memorandum of 1919, was that the jurisdiction of the ministry would extend only to England and Wales, similar but separate arrangements being contemplated for Scotland and Ireland, whereas it was clearly desirable that the Research Committee should be empowered to maintain close touch with the best scientific activities in the whole United Kingdom and, indeed, in the entire Empire. Fortunately, H.M. Privy Council provided—and still provides—a convenient constitutional umbrella for various government standing committees that are independent of the administrative departments, and it was, as the memorandum put it, the only government department with an imperial range. An Advisory Council on Scientific and Industrial Research had already been set up under a special Committee of Privy Council in 1916, to direct the work of the Department of Scientific and Industrial Research, and it was decided that the Medical Research Committee (henceforth to be known as the Medical Research Council) should be given a generally similar constitution.

A Committee of Privy Council for Medical Research was accordingly appointed in March 1920, "to direct the continued performance of the duties heretofore performed by the Medical Research Committee": in fact, the Committee of Privy Council took over the existing Medical Research Committee, which thereupon became the Medical Research Council and was granted a Royal Charter of incorporation under that name. The Lord President—at present Lord Woolton—is chairman of the Privy Council Committee, and he is the minister directly responsible to Parliament for the work of the Medical Research Council. Other members of the committee include the minister of health (as vice chairman) and the ministers in charge of the principal U.K. departments that may also be concerned with questions of public health either at home or overseas; the fact that the minister

of health is vice chairman of this committee provides the only direct constitutional link between the Medical Research Council and the ministry, though naturally there is the closest possible working relationship between them, and the council carries out many research investigations at the ministry's request. The secretary of the Medical Research Council is ex officio secretary of the Committee of Privy Council for Medical Research, and since this ministerial committee very rarely needs to meet (it has, in fact, met only once in history), this means in practice that the council through its secretary has direct access to the Lord President as its minister in Parliament. It may be added that the Agricultural Research Council, set up under the formal direction of another ministerial Committee of the Privy Council in 1931, has a closely similar constitution to that of the Medical Research Council. The fact that the Lord President is the minister responsible for the Department of Scientific and Industrial Research and for the Agricultural Research Council, as well as for the Medical Research Council, is valuable in enabling these three government research organizations to work together on matters of common interest.

If you have been able to follow me through this thicket of constitutional detail, you will, I hope, have realized that the Medical Research Council is in effect a nearly autonomous scientific body maintained by the government. The public funds at the council's disposal are provided annually by the Treasury in the form of a Parliamentary grant-in-aid, and in allocating these in fulfillment of its functions the council is not merely an advisory body but has full executive control. Naturally it is responsible to the Lord President and through him to Parliament as well as to the Treasury and the government auditors, for the proper expenditure of the funds entrusted to it. The council's annual estimate of expenditure is submitted to the Treasury under itemized headings, and if the estimate satisfies the Treasury its approval by Parliament as part of the Civil Estimates is usually purely formal, though it obviously is open to any Member of Parliament to challenge it during the debate on the estimates. Once the grant is approved, the council is virtually free to spend it at its scientific discretion, although the Treasury not unreasonably likes to be consulted in advance about costly commitments of a kind that may extend from year to year; and it requires the council to keep approximately in step with the Civil Service on matters such as salary scales for members of the staff.

There are nowadays twelve members of the Medical Research Council—three lay and nine scientific. The scientific members are appointed by the Privy Council Committee, after consultation with the president of the Royal Society as representing independent scientific opinion in the country, and with the existing members of the council. The scientific members are all distinguished experts who have done important research in their particular branches of medical science; at present they include a physician, a general surgeon, a neurosurgeon, a psychologist, two pathologists, a biochemist, a physiologist, and an anatomist with strong physiological interests. Of the three lay members, at least one must be a member of the House of Lords and one a member of the House of Commons; it is customary for a representative of the House of Lords to be made chairman, and it is a matter of historic interest that the late Chairman of Council, Viscount Addison, who died in December 1951, was, in fact, that same Christopher Addison who had played so important a part in designing the council's constitution; he was happy to be reunited in his old age with the child of his begetting. Members of the council retire in turn at regular intervals, and the scientific members are not eligible for immediate reappointment after serving continuously for four years. This arrangement gives the council a useful turnover of scientific experience. The council appoints its own secretary and other administrative officers, and also its own scientific staff. The present secretary is Sir Harold Himsworth, who succeeded Sir Edward Mellanby in this post in October 1949.

The arrangement by which the individual scientific members serve for only a limited period helps give the council flexibility of outlook and provides a useful variation in the range of technical interests directly represented upon it. Clearly, however, it is impossible for the nine scientific members at any given time to possess detailed knowledge of all the complex and specialized problems of medical science. To counter this difficulty, the council has appointed a large number of expert technical committees to advise it on particular subjects. Some are standing committees, others are appointed on a short-term basis to organize research on a particular subject—such as clinical trials of a promising new remedy. At present there are over thirty standing committees and over twenty *ad hoc* committees, their total membership comprising several hundreds of doctors and other scientists. On some parts of its program the council is advised by joint committees with the appropriate government departments. Thus the Colonial Medical Research Committee, which advises on the promotion of research work bearing on the health and welfare of colonial peoples, is appointed jointly by the council and the Colonial Office.

In promoting research on problems of industrial well-being and efficiency the council is advised by its Industrial Health Research Board and by special committees on occupational health, psychology, toxicology, industrial pulmonary diseases, and many other subjects. Since the beginning of World War II the council, assisted by expert committees, has also undertaken a great deal of research for the defense services on problems affecting the health and efficiency of the fighting man. The council itself meets about nine times a year; its advisory committees, as often as necessary.

I have said that in 1914 the funds available for the work of the Medical Research Committee amounted to about £55,000. The annual Parliamen-

tary grant-in-aid of the Medical Research Council, exclusive of nonrecurrent provision for buildings and special equipment, was £195,000 during the years 1938–43, £295,000 by the end of the second world war, £770,000 in 1948–49, £1,216,000 in 1949–50, and at present it is about £1,666,000. Unfortunately, these rather spectacular increases in the moneys provided by Parliament for medical research since the end of the war have to a large extent been offset by the enormous increase in the costs of services and equipment, as well as by salary increases in the postwar period. The net increase in research resources is therefore much smaller than at first sight appears, but even so it has been remarkable since the end of the war. In the prevailing chilly financial climate, it is certain that the increase cannot be maintained at anything like the same rate in the immediate future, even though Parliament is kindly disposed toward medical research; with steadily mounting expenses, this means, of course, that the council will have less to spend on research projects than it has had recently. That is one of the major difficulties with which we have to contend at the moment.

There are three main methods by which the council supports and subsidizes medical research. First, it employs a scientific and technical staff of its own, of about 1000; of these, approximately 150 are medically qualified, and nearly 300 others have science degrees. Scientific personnel may be employed on a temporary basis for special studies, or they may have permanent engagements, normally tenable until the ages of 60 or 65, with provision for pensions thereafter. The great majority of these men and women work as teams in the council's various research establishments, but a few are attached individually to university departments. Members of the scientific staff are appointed for their attainments or promise in their chosen branch of medical research; within the broad terms of reference of the establishment or department in which they work, they are encouraged, under the guidance of the director, to choose their own problems (and may change these at their discretion) unless—as happens chiefly in the case of temporary appointments—they are recruited specifically to take part in particular projects.

Second, the council makes temporary grants for research projects directly to independent workers in universities, hospitals, and elsewhere. These grants may be made for the personal support of the investigator himself, for the provision of assistance to senior investigators, or for research expenses. Applicants for grants must submit details of their projects for approval, and in reaching decisions the council may take advice from its appropriate expert committee. The grants from the council are ordinarily awarded on an annual basis, but nonrecurrent grants for special research expenses are also made; those made for the personal support of investigators are not normally tenable for a longer total period than three years, though extensions are occasionally allowed. It is against the council's usual policy to make grants to institutions instead of directly to individuals; it does, however, transmit a special block grant of £150,000 from public funds to the research department of the Royal Cancer Hospital, now the Institute of Cancer Research of the University of London.

Third, the council awards studentships and fellowships to enable promising young graduates to be trained under suitable direction in the methods of medical research. These awards are of fairly recent origin, mostly dating from the time of the second world war. It is hoped that they will prove a valuable source of new recruits to medical research. A recent introduction under this heading was a series of Fellowships in Clinical Research to enable well-qualified young men and women who already have had some clinical experience to train in methods of clinical research, this training in appropriate cases including study of the research methods applicable in the basic subject most germane to their particular clinical interests.

In addition to these appointments, which are tenable in the United Kingdom, the council also awards traveling fellowships for work at centers in the United States or elsewhere overseas. The best-known of these awards are the Rockefeller Medical Fellowships, which have been provided from funds generously placed at the council's disposal by the Rockefeller Foundation of New York. This scheme, which was introduced in 1923, has been a great success; a recent survey showed that, of the 147 men and women who have held these fellowships, no fewer than 70 now have academic or research posts of professorial or reader status. A generous donation by the Lilly Research Laboratories has just made possible an additional series of traveling fellowships of generally similar kind, which are tenable in America. The council also awards traveling fellowships for research in tuberculosis from a special benefaction entrusted to it for the purpose. Research and traveling fellowships in ophthalmology and otology have been provided from another special benefaction.

By far the largest of the council's own research establishments is the National Institute for Medical Research. In 1950 the majority of the divisions of the institute were moved from the old building at Hampstead to a new and much more commodious building at Mill Hill, constructed especially for the purpose just before the second world war and equipped in the postwar period. The staff at present working at the institute includes 31 research workers who are medically qualified, and 58 with nonmedical qualifications, in addition to a few administrative officers and the technical, clerical, and maintenance staffs. The first director of the institute was Sir Henry Dale, and it was in the building at Hampstead that he carried out the work on the chemical transmission of nerve impulses for which he shared the Nobel prize in medicine with Otto Loewi in 1936. He was succeeded by the present director, Sir Charles Harington, in 1942. The research work of the institute is divided into ten

main divisions, each under its own head: Biochemistry, Chemotherapy, Bacterial Chemistry, Physiology and Pharmacology, Applied Physiology, Experimental Biology, Bacteriology and Virus Research, Physical Chemistry, Biophysics and Optics, and Biological Standards. The Standards Department—in addition to its national duties in regard to the British Pharmacopoeia and the Therapeutic Substances Act—has important international functions in relation to the activities of the Expert Committee on Biological Standardization of the World Health Organization.

Next to the National Institute, the oldest of the council's research establishments is the Department of Clinical Research at University College Hospital, London. It was here that the late Sir Thomas Lewis, the first director of the department, carried out his historic work on the cardiac arrhythmias and other problems of cardiovascular disease. The success of this department at University College Hospital led the council to set up a Clinical Research Unit on generally similar lines at Guy's Hospital a few years before the war. In the same period they set up a Neurological Research Unit at the National Hospital for Nervous Diseases, London. Among the council's nonclinical establishments which long antedated the second world war are the Statistical Research Unit in London, which was originally part of the National Institute, and the Dunn Nutritional Laboratory at Cambridge.

Since the beginning of the war there has been a remarkable increase in the number of the council's research establishments, and there are now over 40, the majority of them being situated in university departments. The arrangement in such cases is that the professor in charge of the department has the status of "Honorary Director" of the council's Research Unit within it. Each unit consists of a group of picked investigators in the full-time employment of the council, which also provides their research expenses. In the case of the clinical research units in hospitals, the council usually provides the salaries of the director and other members of the research staff, although the remuneration of the directors may be supplemented from other sources. The council also meets the research expenses of the unit, the hospital being responsible for the costs of nursing, feeding, and treating the patients.

Some examples of the council's long list of present research establishments (all with wide terms of reference) include, in addition to the National Institute and the five other prewar establishments already mentioned: a Department of Experimental Medicine (Cambridge); a Tuberculosis Research Unit (London); a Human Nutrition Research Unit (London); Units on Problems of Blood Transfusion, Blood Products and Blood Grouping (London); a Radiotherapeutic Research Unit (London); Otological, Ophthalmological, and Dental Research Units (London); a Chemical Microbiology Research Unit and a Unit for Research on the Molecular Structure of Biological Systems (Cambridge); a Biophysics Research Unit (London); a Cell Metabolism Research Unit (Sheffield); a Department for Research in Industrial Medicine at the London Hospital; an Industrial Injuries and Burns Research Unit (Birmingham); a Pneumoconiosis Research Unit (Cardiff); an Applied Psychology Research Unit (Cambridge); a Social Medicine Research Unit (London); and a Unit for Research on Climate and Working Efficiency (Oxford). In Scotland, there are the Clinical Endocrinology Research Unit at Edinburgh and the Clinical Chemotherapy Research Unit at Glasgow. An important unit outside a university is the Radiobiological Research Unit at the Atomic Energy Research Establishment of the Ministry of Supply at Harwell. Moreover, the council's research units are not confined to the United Kingdom, for it has in the Gambia a Field Research Station which undertakes investigations of tropical diseases and the nutritional requirements of African races; and the council at present shares with the Admiralty the cost of maintaining a Research Unit in Tropical Climatology at Singapore. All these special research units—and many others at home and abroad—form part of the council's own research organization, although they are sometimes shared with other bodies. They are quite separate from the system of research grants to independent workers, in universities and elsewhere, of which there may be as many as 300 or 400 in operation at any given time.

The results of the work carried out in the council's establishments, or by independent investigators financially assisted by the council, are mostly, of course, published as papers in the scientific journals on the authors' own initiative. In addition, however, the council issues through H.M. Stationery Office a series of "Special Reports" giving the results of extensive investigations that cannot be adequately described within the scope of a journal article. Since the war, the council has also issued a series of memoranda describing the results of certain *ad hoc* investigations made with its support, or giving concise summaries of the existing state of knowledge of particular subjects. In accordance with the terms of the council's charter, an Annual Report reviewing the year's activities is presented to Parliament and published. Since the beginning of the war, the reports for a number of successive years have been published together, the latest to appear being that for 1948–50. It is hoped, however, to resume henceforth the prewar system under which the Annual Reports to Parliament did, in fact, appear year by year.

Before concluding, I should refer to an important executive function which the council undertook for the Ministry of Health at the beginning of the second world war and has maintained since: this was the organization of a Public Health Laboratory Service, consisting of an integrated network of bacteriological laboratories throughout the country. It was originally conceived as a wartime emergency service, its primary purpose being to meet the sinister possibilities of bacteriological warfare or of large-scale epi-

demics caused by the disorganization of sanitary services under heavy bombardment from the air. Fortunately, it was not needed for either of these purposes, but it proved so valuable during the war years as a means of rapidly investigating and controlling outbreaks of infectious disease and of bacterial food poisoning that it has been maintained, and indeed expanded, since. The cost of this service is not charged against the grant-in-aid of the council's research program, but is provided separately by action of the Ministry of Health. It is important to add, however, that a great deal of valuable research on problems of bacteriology and epidemiology is carried out by the members of the service, in addition to their more routine duties.

One of the constitutional advantages of the Medical Research Council is that it can cooperate directly with other bodies with similar interests, either at home or abroad. I have already mentioned its cooperation with the Nuffield Foundation and the British Empire Cancer Campaign in the United Kingdom, and I have referred to the invaluable scheme of traveling fellowships for British medical graduates, for which the council has long been indebted to the Rockefeller Foundation. That, indeed, is only one of many activities in which the council has had important help from the Rockefeller Foundation. To take another example, the post of director of the Department of Clinical Research at University College Hospital, London, has for many years been permanently endowed by the foundation, although the council provides the rest of the cost of the department's research program. A particularly interesting form of transatlantic cooperation in the past two years has been the collaborative scheme of research into the value of cortisone and ACTH in rheumatic fever, in which a number of American, Canadian, and British investigators are at present engaged on a freely agreed common plan. Organized by the American Heart Association in the United States and by a committee of the Medical Research Council in the United Kingdom, and financed partly by the U. S. Public Health Service and partly by the council, this study is, I believe, the first example of an international experiment in clinical research. Whatever may be the answers to the scientific questions posed, there can, I think, be no doubt that the scheme itself as a collaborative effort has been an outstanding success, and it is perhaps not too much to hope that it may serve as a model for similar ventures in the future.

I began with a reference to the recent article by Scheele and Sebrell on medical research and medical education, and I promised to end with a brief consideration of some analogies between your medical research organization and ours, and between our respective methods of dealing with similar problems. It seems to me that the seven National Advisory Councils of your Public Health Service approximate in function the Medical Research Council itself, and the eighteen technical "Study Sections" have duties corresponding more nearly to those of the council's expert advisory committees. The emphasis on the value of the Public Health Service research fellowships for expanding the pool of highly trained research manpower corresponds to our own experience with the system of studentships and fellowships that we have instituted since the war. I understand that the research fellowships in medical science awarded by the National Science Foundation will have a similar object.

I have been interested to learn of the discussions taking place within the Public Health Service as to the respective merits of project grants to individuals and block grants to institutions as means of ensuring both intellectual freedom and continuity of support for medical research workers. We believe that our direct staff appointments (inside and outside our own research establishments) and our direct project grants to independent workers are in general the arrangements best suited to conditions in the United Kingdom. (We have in mind in this connection that a prophet may sometimes be without sufficient honor in in his own country, which means in his own university or hospital.) I should remind you, however, that a great deal of both fundamental and applied medical research in the United Kingdom is in fact supported indirectly from the quinquennial block grants made by government to the universities through the University Grants Committee. Clearly, the dominant aim of your arrangements and ours is to provide conditions under which investigators with good ideas and the appropriate skills will have opportunity and facilities to make their discoveries in their own way, whether they work in isolation or as members of a unit or team that includes workers trained in several or many different disciplines. Although planned investigation of particular problems—especially, but not exclusively, military problems—is occasionally necessary, in general we, like you, prefer to avoid the concept of "research to order." Indeed, I believe there has been only one occasion in the long history of the Medical Research Council and its predecessor committee when a research worker was actually ordered, willy-nilly, to study a particular problem. That was in 1916, when Edward Mellanby was—according to his story—positively instructed to work on rickets, although, even here, the methods to be used were left to his discretion. The fact that his study met with triumphant success was no doubt due in the main to his being a very exceptional person. In all ordinary cases the council prefers to leave the choice of problem, within wide limits, to the individual investigator or the director of the unit or team, and to avoid interference with the work while it is in progress, subject to the council's indisputable right to call for a report when necessary. Recently we have tried to minimize even the not-so-insignificant burden of report writing, by telling the directors of our research units that they need submit annually only a very brief report under subject headings, longer and more detailed reports being provided only once in every three years, unless the council thinks it desirable

to call for fuller information in the meantime. This is a rather novel experiment, and it will be interesting to see how it works.

It is reassuring to find that not only individuals, but also the official medical research organizations, in our two countries think so nearly alike as to the best means of achieving their main objective, the advancement of knowledge for the betterment of human health and well-being; and that your avowed aim, like ours, is to supply the means and environment to enable men and women with promising ideas for original research to cultivate those ideas under optimum conditions in their own way, with the minimum of interference or dictation by the executive. That is the cherished, and cherishable, method of the great democracies, and I hope that it always will be.

News and Notes

Scientists in the News

John V. Atanasoff has resigned from the U. S. Naval Ordnance Laboratory, White Oak, Md., where he was assistant to the technical director for fuses, to form The Ordnance Engineering Corporation. The corporation will engage in engineering, evaluation, development, and manufacture of technical and scientific apparatus, especially ordnance devices. The plant is located near Rockville, Md. Officers of the new company are John V. Atanasoff, president and general manager; Arthur C. Ross, vice president; David W. Beecher, vice president and assistant general manager (formerly of the Acoustics Division, U. S. Naval Ordnance Laboratory); Alice C. Atanasoff, secretary; and Frank C. Kramer, treasurer (formerly on the technical director's staff of NOL).

Eugene N. Beesley has been named an executive vice president by the board of directors of Eli Lilly and Company. He formerly held the post of vice president in charge of administration of the pharmaceutical firm.

Lester R. Dragstedt, chairman of the Department of Surgery of the University of Chicago Medical Center, has been named Thomas D. Jones distinguished service professor of surgery at the university. He succeeds the late **Dallas B. Phemister** in the professorship, which was established in 1940 to honor the late Chicago industrialist, who made large gifts to the endowment of the university medical center when it was first being planned in 1917.

Louis I. Dublin, second vice president and statistician, has reached retirement age, and will retire from the Metropolitan Life Insurance Company on Jan. 1, 1953. **Edward A. Lew,** now associate actuary, will be appointed associate actuary and statistician, as successor to Dr. Dublin, and **Mortimer Spiegelman,** now assistant statistician, will be appointed associate statistician.

Paul Engel, formerly professor of biology, anthropology and psychology at La Universidad Libre de Colombia, Bogotá, and professor of pharmacology at the National University of Colombia, has received an honorary D.Sc. degree from Universidad Libre de Colombia. Dr. Engel is now on the research staff of Laboratorios LIFE, Quito.

Fred L. Fitzpatrick has been made head of the Department of Natural Sciences at Teachers College, Columbia University. He was on the faculties of the Colorado College of Education and Coe College before joining the Teachers College staff as an associate professor of science in 1931.

Samuel S. Goldich, of the U. S. Geological Survey, is in Brazil for a reconnaissance examination of the bauxite deposits of the Pocos de Caldas area in Minas Gerais. Dr. Goldich's examination will be conducted in cooperation with the geologists of the Departamento Nacional da Produção Mineral, who have been engaged in the study of this area for some years. This investigation is a part of a long-term program of cooperative investigation of Brazilian mineral deposits conducted jointly by the Geological Survey and the Brazilian DNPM under the auspices of TCA.

Harrison F. Gonnerman and **William Lerch,** of the Portland Cement Association, received the Sanford E. Thompson Award at the 50th anniversary meeting of the American Society for Testing Materials. The award was won by the Gonnerman-Lerch paper on the subject "Changes in Characteristics of Portland Cement as Exhibited by Laboratory Tests over the Period 1904 to 1950." The paper was presented at the annual meeting of the ASTM last June. Mr. Lerch is administrative assistant in the Research and Development Division, and Mr. Gonnerman is assistant to the vice president for Research and Development in the Portland Cement Association.

Alonzo G. Grace, professor of education at New York University, has been appointed associate dean of the university's School of Education. Professor Grace, who joined the NYU faculty in 1951 as director of the Division of Advanced Studies, will direct a new program under the Division of the Scientific Study and Advancement of Education, which will go into operation in the fall.

William A. Hinton has retired as chief of the Department of Clinical Laboratories at the Boston

Dispensary, after 36 years of service. He will continue to serve in a consulting capacity and will retain his position as one of the directors in the Institute of Laboratories of the Massachusetts Department of Public Health. **Mario Stefanini** has been appointed acting chief to succeed Dr. Hinton. Dr. Stefanini holds appointments currently as physician in the New England Center Hospital and associate director, with **William Dameshek,** of the Blood Bank and the Hematology Research Laboratory. He is also associate research professor in medicine at Tufts College Medical School.

The appointment of **Wilbur M. Hurst** and the retirement of **George R. Boyd** as head of the Division of Mechanical Processing of Farm Products, have been announced by the U. S. Department of Agriculture. Mr. Hurst has been in the department since he entered as a junior agricultural engineer in 1926. Mr. Boyd entered the department in 1908 as an agent in irrigation investigations for the Office of Experiment Stations.

Stewart S. Kurtz, Jr., has been named technical associate in Sun Oil Company's Research and Development Department, where he will be staff assistant to J. Bennett Hill, director of the Chemical and Engineering Division. Since 1942 Mr. Kurtz has served as manager of the company's Chemical Research Laboratory at Norwood, Pa. He will be succeeded in this position by **C. L. Thomas.**

Alexander R. Lindsay has been elected vice president in charge of research and engineering in the Budd Company to succeed **G. M. Barnes,** who is retiring. Mr. Lindsay, who has been with the Budd Company since 1937, formerly was chief engineer of its automotive division.

Vernon W. Lippard has been named dean of the Yale School of Medicine, succeeding **C. N. Hugh Long,** who is giving up his administrative duties in order to devote full time to research and to serve as chairman of the Department of Physiology. Dr. Lippard will go to Yale from the University of Virginia, where he has been dean of the Department of Medicine since 1949. From 1946 to 1949, he was dean of the School of Medicine at Louisiana State University, and from 1939 to 1946, associate dean of the College of Physicians and Surgeons at Columbia University.

Robert L. McMurtrie has become chief of the Lignite Branch of the Region V Fuels Technology Division and superintendent of the Charles R. Robertson Lignite Research Laboratory, Bureau of Mines, in Grand Forks, N. D. He will work directly under Alex. C. Burr, chief of the Bureau's Region V Fuels Technology Division. Mr. McMurtrie will take a six months' training course in Washington, D. C., and at bureau field installations concerned with coal research before assuming the duties of his new position.

John Milton Miller has retired as deputy director of research of the Naval Research Laboratory of the Office of Naval Research. He has spent 45 years in the fields of electricity and radio communications, 30 of them with the government. **Claud Edwin Cleeton,** head of the Security Systems Branch of Radio I, has been selected to succeed Dr. Miller as superintendent of Radio I Division. Dr. Cleeton joined the Naval Research Laboratory as physicist in 1936. Since 1946, he has continued this work for the Navy as head of the Security Systems Branch of Radio Division I at NRL.

Bernard L. Oser, director of Food Research Laboratories, Inc., Long Island City, is attending the second International Congress of Biochemistry in Paris and the second International Congress on Analytical Chemistry at Oxford; he will also visit academic and industrial laboratories in Israel.

Linus Pauling, chairman of the Division of Chemistry and Chemical Engineering at California Institute of Technology, has left for a six-week visit to France and England. In Paris, he attended the second International Congress of Biochemistry. He is honorary president of the Section on the Biogenesis of Proteins. In England Professor Pauling will attend a discussion meeting of the Faraday Society, of which he is a member, on the physical chemistry of proteins, and will confer with Lawrence Bragg and other British scientists on problems of protein structure in laboratories in Cambridge, Oxford, Leeds, London, and at the Rothamstead Experimental Station. From England Dr. and Mrs. Pauling will fly to Toronto for another meeting of the Faraday Society, Sept. 8–9. Last May Dr. Pauling was to attend a discussion meeting of the Royal Society (London) on the structure of proteins and was to give a special lecture on that subject before the Royal Institution of Great Britain. The Department of State denied him a passport, and the trip was cancelled. Now, in its mysterious way, the Department finds it can issue a passport "on the basis of new evidence and re-evaluation of old."

Simon Stickgold, former chief of the Division of Special Services of the Illinois Public Aid Commission, has been appointed senior research analyst in the Research and Reporting Service of the National Society for Crippled Children and Adults. Serving on the Illinois Public Aid Commission's executive staff since 1945, Mr. Stickgold has directed the Department of Investigations and Frauds, a division he organized four years ago. During that time his staff conducted more than 1700 investigations. Prosecution of frauds on state relief rolls through this unit has resulted in a conviction record of 95.2% and claims of restitution of more than $1,250,000.

The tenth annual achievement award of the American Association of University Women has been conferred on **Lily Ross Taylor,** retiring dean of the Bryn Mawr College Graduate School. Dr. Taylor was cited for "the diversity of her talents as an administrator, author, and teacher who in a very special way has

made learning a dynamic thing, and also as a scholar who has made her wisdom useful in the ordinary business of life." She has been named professor-in-charge of the School of Classical Studies of the American Academy in Rome for next year.

Rudger H. Walker has been named as assistant director of the Office of Foreign Agricultural Relations, succeeding **Ross E. Moore,** who is joining the Technical Cooperation Administration of the Department of State as director of Point IV activities in Mexico. Dr. Walker, who has been chief of OFAR's Technical Collaboration Branch since March 11, will be succeeded by **Glenn L. Taggart,** who has been assistant chief of the branch since October 1950. Dr. Walker was dean of the School of Agriculture and director of the agricultural experiment station at Utah State College from 1938 to 1952. Dr. Taggart has long been identified with the department's technical assistance activities.

Norman Wengert, of Milwaukee, has been appointed professor and chairman of the Social Science Department at North Dakota Agricultural College, succeeding **William C. Hunter,** who has retired. During the past year, Dr. Wengert has been in Washington, D. C., with the Department of the Interior. For four years, he was on the faculty of the City College of New York, besides serving as visiting lecturer at the University of Wisconsin and at Wayne University.

William E. Wrather, director of the U. S. Geological Survey and treasurer of the AAAS, will head the delegation appointed by the Executive Committee to represent the Association at the Algiers meeting of the International Geological Congress Sept. 8–15. Other official delegates are Richard M. Foose, president of the Lancaster (Pa.) Branch of the AAAS and also official representative of the American Institute of Mining and Metallurgical Engineers, and Kirtley F. Mather, AAAS retiring president.

Benjamin P. Young, of the Cornell Zoology Department, has been appointed professor emeritus of zoology. He joined the Cornell faculty in 1919.

Education

The **University of Alaska** has just dedicated the Brooks Memorial Mines Building in honor of the late Alfred H. Brooks. The distinguished scientist, member of the Geological Survey, explorer, and historian, was honored at ceremonies commemorating the 50th anniversary of the discovery of gold in the Fairbanks area. Dr. Brooks began his work with the USGS in 1888; in 1895 he and five other young geologists founded the Association of Ambitious Assistants, which later became the Pick and Hammer Club. In the spring of 1898 Dr. Brooks was one of a group that explored the lower White River and a part of Tanana River, about which very little was then known by white men. Thus began his career of more than 25 years in Alaskan affairs. Dr. Brooks was born in Ann Arbor, Mich., July 18, 1871, and died Nov. 22, 1924.

The curricula in engineering in the **University of California** at Davis will be offered for the first time to freshman students enrolling for the 1952–53 academic year. The new College of Letters and Science, now entering its second year, plans to expand its work in several fields, so that it will eventually offer majors in 11 fields and other work in the arts, humanities, and sciences that will support the main courses.

Winthrop College, the South Carolina college for women, has appointed John A. Freeman and James C. McMahon, Jr., to the Department of Biology. Mary Schuchart, of the same department, is retiring this month.

At the **University of Wisconsin,** Frederick E. Shideman has been named professor of pharmacology and toxicology to replace O. S. Orth, who has been transferred to the new Department of Anesthesia. Harry Waisman, of the University of Illinois College of Medicine, has been appointed associate professor of pediatrics. Other changes involve the replacing of K. J. Arnold, who was head of the computing service, by Preston C. Hammer, of Los Alamos; leaves of absence for J. Theodore Morgan (economics), to continue as adviser to the Central Bank of Ceylon, and for J. B. Wilson (agricultural bacteriology) to continue his work at Dugway Proving Ground. Robben W. Fleming, director of the University Industrial Relations Center since its founding, has resigned to head the Institute of Labor and Industrial Relations at the University of Illinois. James G. Moore, former head of the Department of Horticulture, is retiring this year.

Grants and Fellowships

The **American Heart Association** is accepting applications for Research Fellowships and Established Investigatorships, which should be submitted by *Sept. 15,* and for Research Grants-in-Aid, which may be filed up to *Dec. 1.* Under a new scale, stipends for the fellowships range from $3500 to $5500, and for the investigatorships from $6000 to $9000. Grants-in-aid, awarded to nonprofit institutions, vary in amount, usually not exceeding $10,000. Information and forms may be obtained from the medical director of the association, 1775 Broadway, New York 19.

The **Fund for the Advancement of Education** has allocated more than $2,000,000 to establish a new fellowship program for high school teachers, which will be initiated this fall. It will enable some 400 teachers to be relieved of their teaching duties for the coming academic year so that they may spend their time on self-designed projects to broaden their liberal education. All inquiries should be addressed to the National Committee on High School Teacher Fellowships (Lester Nelson, chairman), 575 Madison Ave., New York 22.

Illinois Institute of Technology will grant 100 scholarships, valued at one-half tuition, to veterans entering the institute in either September 1952 or

February 1953 under the new Korean G. I. Bill. The scholarships will be for one year and are renewable.

Philco Corporation has provided a grant of $18,000 for three scholarships of $1500 each annually for the next four years at Lehigh University, for the training of engineering students.

A. H. Robins Co., Inc., of Richmond, Va., has made a grant of $5500 to Leon L. Wiesel, Brooklyn Hospital, Brooklyn, N. Y., for further investigation of the synergistic action of *p*-aminobenzoic acid and cortisone in the treatment of rheumatoid arthritis.

The **Sarah Mellon Scaife Foundation** has supplied funds to the Mellon Institute for a fellowship to conduct systematic studies of standardization and its applications in science, engineering, production, and marketing. The projects will be organized and supervised by Dickson Reck, lecturer in business administration at the University of California.

War Memorial Scholarships have been awarded by **Westinghouse Electric Corporation** to four teen-age sons of employees. The scholarships, established in 1919, are awarded annually so that the winners may continue their undergraduate study in engineering or physical science.

The **John Hay Whitney Foundation**, 30 Rockefeller Plaza, New York, has announced its first six awards to retired professors who will continue teaching at small selected liberal arts colleges. Under this new program, the Whitney Visiting Professors in the Humanities, the foundation pays the salaries and the college provides housing. The foundation is establishing a registry of professors in the humanities, who, although retired, still wish to teach. Among the new appointees were three language professors, one history professor, one professor of classics, and one professor of sociology—Arthur Evans Wood, of the University of Michigan, who will teach next year at Wittenberg College.

In the Laboratories

AiResearch Manufacturing Company, Los Angeles, has sent Donald S. Campbell to London as its technical representative on assignment to the Joint Advisory Military Assistance Group. He will serve as adviser to JAMAG and as an instructor to key air force and commercial airline personnel of Title I MDAP countries. Ivan Speer has been transferred as engineering manager to AiResearch's Arizona Company, and S. K. Andersen has been promoted to chief engineer at the main plant in Los Angeles.

A $4,500,000 rolling mill will be installed at the Davenport, Ia., works of **Aluminum Company of America** late next year. The equipment will be designed, installed, and operated by ALCOA under a lease arrangement with the USAF Air Materiel Command, and the Air Force will have first call on production of the new mill.

Armour Research Foundation has announced expanded activity in operations research, with the appointment of Thomas E. Caywood, senior operations research officer for the Institute for Air Weapons Research at the University of Chicago for the past five years. As the operations research member of an RDB committee, he is at present studying rockets. In other departments of the foundation James Cooperman, development chemical engineer for Southern Natural Gas Co., has been appointed research chemist, and Harry C. Ehrmantraut, of the Toni Co., has been appointed a research biochemist.

A new **Laboratory of Astrophysics and Physical Meteorology** has been established at The Johns Hopkins University. John D. Strong has been named director, as well as professor of experimental physics.

Arthur S. La Pine & Company have opened their new plant at 6001 S. Knox Ave., Chicago. The 37,000 square feet of space contains a large laboratory for the testing and inspection of new equipment, and a machine shop for the manufacture and repair of scientific equipment.

Arthur D. Little, Inc., has added the following scientists to its staff: Frank W. Maurer (physiology); George Robinson (mechanical engineering); Stanley Arasim (business research); John C. Stephenson (consulting work with overseas clients); and Marvin C. Tobin (physical chemistry). The Little firm will move its Mechanical Division to a new and larger building that is now being built in the West Cambridge, Mass., industrial area.

Walter L. Hardy has joined **Foster D. Snell, Inc.**, as director of package engineering. The Package Engineering Division will carry out research and development of packaging materials and procedures, corrosion and its prevention, prevention of mold and fungus deterioration, shock and vibration studies, and package and package material evaluations.

Meetings and Elections

At the annual meeting in New York of the **American Library Association**, Flora B. Ludington, of Mount Holyoke College, was named first vice president and president-elect for 1953. Robert B. Downs, director of the University of Illinois Library and Library School, was installed as president, succeeding Loleta Dawson Fyan.

Edward J. McCormick, of Toledo, Ohio, has been made president-elect of the **American Medical Association**; Leo J. Schiff, of Plattsburg, N. Y., vice president; and James R. Reuling, of Bayside, N. Y., speaker of the House of Delegates. J. J. Moore and George F. Lull were re-elected treasurer and secretary, respectively. E. P. Jordan and George M. Pierson are the AAAS Council representatives.

The **American Psychiatric Association**, meeting in Atlantic City, named Kenneth E. Appel president-elect; R. Finley Gayle, Jr., secretary, and Howard W. Potter treasurer.

The **Medical Library Association** has elected the following officiers: president, W. D. Postell; vice president, Marion Dondale; honorary vice president, Emerson Crosby Kelly; secretary, Louise Lage; treasurer, Helen Woelfel. The next meeting of the organization will be held in Salt Lake City, June 16–19, and in 1954 the association will meet in Washington, D. C.

The **Nebraska Academy of Sciences** has elected the following officers: president, W. W. Ray; vice president, I. L. Hathaway; secretaries, C. B. Schultz and H. L. Weaver; treasurer, C. E. Rosenquist; assistant to the secretary and treasurer, Mary L. Hanson.

An **Operations Research Society of America** was organized at a recent meeting at Arden House, in which experts in physics, chemistry, biology, mathematics, economics, and statistics assembled to pool their knowledge in an attempt to promote the application of scientific methods to complex business and military problems. Philip Morse, of MIT, was elected president, and Robert H. Rinehart, of Case Institute, vice president.

The **Society of Women Engineers** has elected Lillian G. Murad president, Katharine Stinson vice president, and Emma C. Barth and Margaret M. Ross secretaries. The following were elected to the Board of Directors: Dot Merrill, Miriam K. Gerla, Doris M. McNulty, and Aileen C. Fong.

The **Southern Association of Science and Industry,** meeting at Winston-Salem, N. C., elected A. B. Paterson president and A. P. Black and Frank J. Soday vice presidents; George D. Palmer and Alva G. Maxwell were re-elected secretary and treasurer, respectively. New trustees are J. E. Davis, A. V. Wiebel, Robert C. Miller, and Enoch H. Brown. Paul M. Gross, vice president of Duke University, received the association's annual award for distinguished service to the South. The association has just become affiliated with the AAAS.

Miscellaneous

The **Agricultural Research Administration** reports among its many foreign visitors K. Norrish (Australia); Paulo B. Rebello and V. L. Xavier (Brazil); M. A. Ragab (Egypt); P. V. Laakso (Finland); G. Boldrini (Italy); H. J. de Fluiter (Netherlands); J. Marrero (Puerto Rico); C. M. Sanchez (Venezuela); Wan Hsiung (Formosa); T. Buchelos and J. Raftopoulos (Greece); and F. Accame (Peru).

Under the sponsorship of the **American Museum of Natural History** and the **Explorers Club,** John C. Pallister and Mrs. Pallister will spend three months in remote sections of the Yucatán Peninsula searching for specimens of insects native to that area. In addition, Mr. Pallister intends to make a photographic study of some of the unfamiliar aspects of the animals and people of Yucatán.

Through an arrangement sponsored by the Viral and Rickettsial Registry, and by courtesy of S. E. Luria, of the University of Illinois, the **American Type Culture Collection,** 2029 M St., N. W., Washington 6, D. C., has received a set of the T-phages, 1 to 7, of *Escherichia coli.* Specimens of these phages, together with the companion bacterial culture, strain B, can now be furnished to investigators in this field.

Marston Bates, formerly of the Rockefeller Foundation, has joined the faculty of the University of Michigan as professor of zoology.

A gold medal and citation were awarded posthumously to **Howard W. Blakeslee** by the American Medical Association last June. Mr. Blakeslee, Associated Press science editor, died in May. The AMA award was created to honor "a distinguished layman who has served to advance the ideals of American medicine and who has contributed notably to the public welfare." The first award was made in 1948 to Father Alphonse Mary Schwitalla.

A **Clearinghouse on Current Morbidity Statistics Projects** has been established under the auspices of the Public Health Conference on Records and Statistics. The clearinghouse will annually canvass investigators in various fields for reports of studies or surveys in progress, and lists of new projects will be released from time to time.

The **New Zealand Department of Scientific and Industrial Research** recently issued its 25th annual report for the year ending March 31, 1951 (available at 1s. 6d. from the Government Printer, Wellington). During the year £903,550 was expended—£316,296 for research, and the balance for such regular services as the Dominion Physical Laboratory, the Geological Survey, etc. Universities, agricultural colleges, and research associations received grants totaling more than £60,000. A great deal of the research was applied to problems in the well-established pastoral, agricultural, and industrial activities for which New Zealand is well known, but the programs contained some unique projects, among them a study aimed to utilize the geothermal steam and hot water of the Wairakei volcanic district for power and industrial purposes. There is the customary preoccupation of government reports with the need to justify continued support, but the scope and caliber of the work done in 1950–51 should convince any body of lawmakers that science and New Zealand economy are intimately linked.

Chemicals wanted by the **Registry of Rare Chemicals,** 35 W. 33rd St., Chicago 16, Ill., are: tungsten disulfide; boron trimethyl; potassium perselenate; calcium thiomalate; triethyl bismuth dibromide; 1,11-undecanedioic acid; ceryl alcohol; iododichlorophosphine; cyclohexylphenyl ketone; 2,5-xylyl hydrazine; lysergic acid; sphingosine; pyrithiamine; secretin; phytase; pitessine; oxyindol; coronene; N-methyl neosynephrine; and coproporphyrin III.

Technical Papers

Ability of Mice of the Genus *Peromyscus* to Hear Ultrasonic Sounds[1]

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When a peromyscus is exposed to a sudden sound it will nearly always react by a movement of its ears. The responsiveness of an individual to sounds, therefore, can be ascertained by watching it closely while sound of a particular frequency and intensity is turned on and off. This method has been used by many previous authors.

Most of the peromyscus used in these studies have belonged to various races and racial hybrids of the deermouse (*Peromyscus maniculatus*), but we have also tested the hearing range of a few individuals of the juniper-mouse (*P. nasutus*).

Two sound sources were used in our experiments: (*a*) a 15-in. coaxial loud-speaker, which covered the range from 500 to 16,000 c/sec, and (*b*) a special crystal transducer, which operated at frequencies from 10 to 100 kc/sec. An oscillator connected to an amplifier provided the necessary electrical input to these instruments.

The intensities of the sounds produced by the transducer or speaker were measured by a circuit consisting of a calibrated condenser microphone, preamplifier, wave filter, amplifier, and oscilloscope. The sounds produced were nearly pure tones, as shown by a close approach of the vibrations to sine waves. Sound pressures used in testing were mostly adjusted to 1, 5, 10, or 20 dynes/cm^2 at the position of the mouse's ear, but lower or higher intensities were sometimes applied.

When the sound-producing apparatus was suddenly turned on or off, an audible click was produced. In order to avoid the possibility that the animals might react to this click, rather than to the fundamental frequency, an electronic click-control device was inserted into the sound-producing circuit. This device operated to initiate the sound at a very low intensity, to increase the intensity rapidly, and then to approach the maximum slowly, the plot of time against intensity simulating a logistic curve. The apparatus was usually adjusted so that 1½ sec elapsed from the time the controlling key was depressed until the sound reached the maximum intensity for which the apparatus was adjusted. Operation of the sound-controlling key with the current turned off produced no sound detectable by human ears and caused no response by the animals.

[1] This investigation was supported in part by a research grant (MH-375) from the National Institute of Mental Health, National Institutes of Health, USPHS. Much of the equipment used in the study was provided by grants from Philip M. Blossom.

The mouse being tested was held in a small cage of ⅓-in. mesh wire screen, placed directly in front of the sound source. Sponge rubber was placed under the cage and also under the sound-producing instruments. The testing room was relatively free from extraneous sounds, but was not especially sound-deadened.

That the stimuli which induce movements of the pinnae are received in the internal ear was proved by testing a deermouse before, during, and after its ear canals had been closed with plugs of cotton soaked in vaseline. The responses were greatly reduced when the ear canals were plugged. Additional evidence that ear movement is a dependable measure of hearing ability for the deermouse was obtained by training two deermice to give a conditioned response to the sound signals. These animals were trained to touch a pencil inserted through the side of the cage whenever a sound stimulus was applied, and thus to avoid a slight electric shock. At the frequencies tested between 10 and 65 kc/sec, these mice responded by ear twitches to exactly the same frequencies and intensities to which they gave the conditioned response.

Still further evidence that the animals actually hear and are affected by the sound frequencies to which they respond by ear movements was given by the reactions of individuals belonging to the *P. m. artemisiae* strain of epileptic deermice. The mice of this strain go into convulsions when exposed to sound stimuli of certain kinds (*1, 2*). Individuals of this strain have gone into dashing seizures or into strong convulsions when exposed to frequencies of 10, 12, 16, 20, 22, 24, 26, 30, 40, 50, and 80 kc at sound pressures of 30 dynes/cm^2 or less. This demonstrates not only that these susceptible mice can hear a wide range of frequencies, but that the abnormal behavior also may be induced by exposure to frequencies included in this same wide range.

A mouse whose ear canals were plugged failed to exhibit any epileptic behavior when exposed to the sound produced by jingling keys, although this individual had a severe convulsion when exposed to the same stimulus after the plugs in its ears had been removed.

The pure tones produced by our apparatus, however, are less efficient for inducing convulsions in these susceptible mice than are the mixed sounds produced by the jingling of keys. Numerous individuals of this strain have failed to show any abnormal behavior when exposed to nearly pure tones at sound pressures as high as 70 dynes/cm^2 at a frequency of 20 kc, although these same individuals have had convulsions when exposed to the jingling of keys. We have not been able to measure the pressures of the mixed sounds produced by the jingling of keys. It is possible, therefore, that the greater effectiveness of jingling keys over pure tones in inducing convulsions in susceptible peromyscus may be due, at least

in part, to a greater total sound intensity for the mixed sounds.

Using the equipment and the methods above described, individual peromyscus afflicted with the *artemisiae* type of epilepsy showed ear movements in response to sound frequencies from 500 to 95,000 c/sec when tested at ages between 25 and 70 days. The band of frequencies from 5 to 16 kc/sec is the most effective for eliciting ear movement in the mice of this strain. Decrease in effectiveness is fairly abrupt for frequencies below 4 kc/sec. Above 16 kc/sec, the effectiveness of the sound in inducing a response decreases gradually with increase of frequency. With each increase in sound pressure certain mice show a broadening of the band of frequencies which will evoke a response.

It is possible that with increased sound pressures, responses could be obtained to higher and lower frequencies than those here reported. Furthermore, the mice may hear frequencies higher and lower than those to which they respond by ear movement. All the observers who have worked for any length of time with these mice have noted that, when presented with sounds just beyond the range which induces definite ear movement, some animals may respond by turning the head or by cessation or beginning of body movement. Much more study will be needed to ascertain accurately the audibility curve of these animals.

As they grow old the hearing ability of most of the epileptic individuals decreases, especially for the higher frequencies, but with much variability between individuals. Certain epileptic individuals ultimately become completely deaf, as is shown by their failure to respond to sounds of any kind. Such deaf individuals do not go into convulsions when exposed to those sonic or ultrasonic sounds we have produced. The relationship between hereditary susceptibility to audiogenic seizures and degree of responsiveness to sonic and ultrasonic sounds, however, needs further investigation.

The epileptic deermice whose hearing ability is here described were of mixed racial stock, in whose ancestry the subspecies *P. maniculatus artemisiae* and *P. m. blandus* were prominent. Young individuals of a strain of the subspecies *bairdi* from near Ann Arbor, Mich., are generally similar in their hearing range to the young racial hybrids above described. In *bairdi,* audiogenic seizures are absent. At frequencies between 5 and 60 kc, higher intensities of sound are required on the average to produce a response by the small-eared *bairdi* than by the generally larger-eared racial hybrids. Young individuals of a strain of *blandus* from New Mexico, on the average, failed to respond by ear movements to ultrasonic sounds of as high a frequency and on the whole were less responsive to pure tones than the young epileptic individuals of mixed racial ancestry.

Three individuals of *P. nasutus* from a hybrid stock resulting from a cross between the subspecies *nasutus* and *griseus* have responded by ear movements to frequencies as high as 100 kc/sec. In general these animals exhibited a slightly greater responsiveness to high frequencies than members of the species *maniculatus.* It is possible that this greater responsiveness may be related to their very large ears. Further studies are needed to compare the hearing ability of individuals, races, and species which differ in the sizes of their external ears.

No consistent difference in hearing ability between male and female peromyscus has been discovered.

The hearing range of peromyscus evidently is somewhat similar to that of certain rodents tested by Schleidt (*3*). It is to be noted also that at least some peromyscus can hear ultrasonic sounds within the same general frequency range that is used by bats for echolocation (*4*). It is not yet known, however, whether a peromyscus can produce ultrasonic sounds over the range of frequencies that it can hear.

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Manuscript received March 10, 1952.

Infrared Spectrophotometry as a Means for Identification of Bacteria

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Infrared absorption spectrophotometry is finding increasing use in the biological sciences. Spectra have been published of dried whole tissues (*1, 2*), individual dried cells (*3*), muscle cells in Ringer's solution (*4*), and cellular components (*5, 6*). Randall *et al.* (*7*) have published the spectra given by organic solvent extracts of *Mycobacterium tuberculosis* and correlated the spectra with biological properties such as virulence. The purpose of the present investigation was to determine whether infrared spectra of whole bacteria could be used for identification of the species and perhaps the strain of the organism. The results clearly indicate that considerable differentiation of both is possible by this approach.

Dried films of the organisms were prepared by taking a few colonies from an agar plate, spreading them with a rubber policeman over the surface of a silver chloride plate, and allowing the film to dry. When pathogenic bacteria were used, the dried film was covered with another silver chloride plate, and the edge sealed with cellophane tape to prevent aerosol production from a flaking-off of the dry film. Interference patterns occasionally observed when using two plates were eliminated by placing a piece of paper or tape on one side between the plates so that they were not parallel. Some preliminary work was done

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using washed organisms grown in broth culture, but this technique was discontinued in favor of the simpler colony smear technique. With most organisms, the smears dried to give smooth transparent films, from which excellent spectra were obtained. With many spectra the transmission at 5.5 μ was above 90%, and at 6.05 μ dropped to below 5%. Some organisms, however, especially those with a high lipid content, produced films exhibiting much general light scattering; hence they had a lower transmission at 5.5 μ and consequently less contrast between the transmissions at 5.5 and 6.05 μ. The transmission at 5.5 was taken as a measure of the quality of the film, and the transmission of the carbonyl band at 6.05 was taken as a measure of the thickness of the film. Most spectra considered had transmission values of greater than 90% at 5.5 μ and less than 10% at 6.05. The thickness of the films was not a critical factor, because the differentiation was based on qualitative differences in the shapes of the absorption bands. The Perkin-Elmer Model 21 Double Beam infrared spectrophotometer was used for recording the spectra.

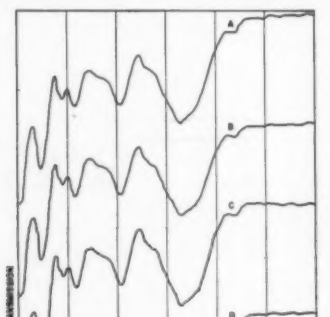

FIG. 1. Spectra of separate cultures of *Serratia marcescens* cultured for 24 hr on fortified tryptose agar.

Since the infrared absorption spectrum of a specimen is a function of the chemical composition, it was necessary to control such conditions as culture medium, age of culture, and temperature of incubation, since these are known to affect the chemical composition of organisms. Experimentally, it was demonstrated that these variables alter the infrared spectra in varying degrees, depending upon the species of the organism.

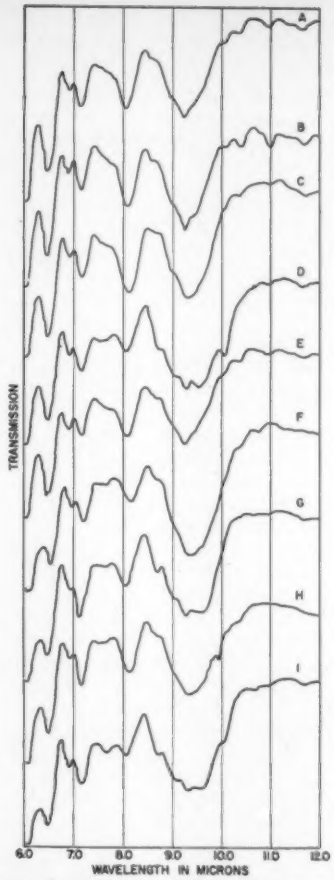

FIG. 2. Spectra of different species cultured for 24 hr on fortified tryptose agar: (*A*) *Escherichia coli*; (*B*) *Pseudomonas aeruginosa*; (*C*) *Micrococcus pyogenes* var. *aureus*; (*D*) *M. rosaceous*; (*E*) *Aerobacter cloacae*; (*F*) *Bacillus subtilis*; (*G*) *B. megatherium*; (*H*) *B. globigii*; (*I*) *Sarcina lutea*.

The most informative spectral range was found to be that between 5.5 and 12.0 μ.

The first problem was to determine the degree of reproducibility. Fig. 1 shows spectra of a number of separate cultures of *Serratia marcescens*. Although, because of variations in the thickness and physical homogeneity of the films, these curves are not all identical, they are qualitatively very similar. Fig. 2 shows spectra of 9 organisms typical of approximately 30 studied. These were cultured 24 hr at 37° C on fortified tryptose agar. Spectra of almost all organisms have the same major absorption bands, but the relative intensity varies from one species to another; this, plus minor absorption bands, varies the shape of the broad bands and the intervening regions between these bands. Although the differences were somewhat subtle in some cases—as, for example, be-

tween *Escherichia coli, Pseudomonas aeruginosa,* and *Aerobacter cloacae*—they were sufficiently consistent to differentiate the species studied to date. Infrared spectra do not always group species as in the Bergey classification. For example, *Pseudomonas* (Family II) organisms and *Escherichia* (Family X) have similar spectra, whereas *Micrococcus rosaceous* and *M. pyogenes* var. *aureus* (Genus I, Family V) have very different spectra.

In addition to differentiation of species, it was possible to differentiate strains of *Bacterium tularense*

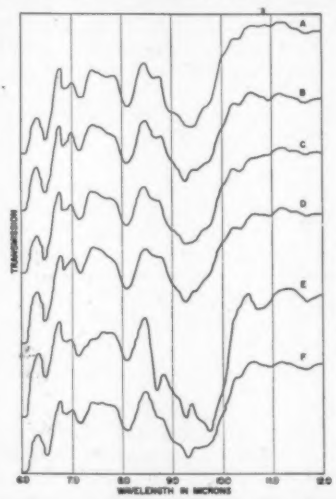

FIG. 3. Spectra of various strains of *Bacterium tularense* cultured for 24 hr on tryptose agar: (*A*) *Schu* S_3; (*B*) *Schu* NS_3; (*C*) Jap S_2; (*D*) Jap S_2^{ss}; (*E*) 38 NS_2; (*F*) 38 S_2.

(Fig. 3). Spectroscopic differentiation of the *Schu* S_3 smooth strain and the Jap S_2 smooth strain (*8*) is somewhat uncertain, but the differences between other strains studied are quite obvious. Spectra of all strains of *B. tularense* are characterized by a sudden drop in transmission at 6.80 μ, producing a clearly marked minimum at that point. The spectra of all other organisms thus far observed have a minimum transmission at 6.90 instead of 6.80 μ.

The use of infrared absorption spectra as an aid to identification appears promising. The prerequisite for such identification is a catalogue of spectra of organisms cultured under controlled conditions.

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Manuscript received March 10, 1952.

Effect of Penicillin on Streptomycin-dependent Variants in *Escherichia coli* Populations

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The penicillin method for the isolation of biochemically deficient mutants (*1–3*) has been applied to the problem of the origin of streptomycin-dependent variants of *Escherichia coli*. If dependent cells arise spontaneously in an actively growing culture of normal bacteria, they should soon stop growing, since no streptomycin is present and since their requirement for this substance has been shown to be highly specific. If this cessation of growth occurs while the remainder of the population is still growing actively, penicillin may be expected to kill the normal cells and spare the streptomycin-dependent ones, as in the usual isolation of biochemically deficient mutants by this method. If, on the other hand, streptomycin-dependence represents an adaptation to the antibiotic, no reason is known why the precursors in the normal population before contact with streptomycin would be uniquely insensitive to the bactericidal action of penicillin.

A smooth, motile strain of *E. coli* was used, which behaved typically in the usual series of characterization tests. The organism was grown from small inocula at 37° C in Difco nutrient broth with 0.2% added glucose. The inoculum size was estimated by turbidimetry and viable counts. When the desired degree of growth had been reached (usually $1–3 \times 10^9$ cells/ml), the culture was centrifuged and resuspended in fresh nutrient broth with glucose. A viable count was made, and 0.3 ml implanted onto each of 6 nutrient agar plates containing streptomycin (*SM*), 10 μg/ml. These plates had been previously dried so that the implant fluid would be absorbed within 30 min at room temperature. Penicillin (300 u/ml) was added to the remainder of the resuspended culture at 37° C; the culture was then incubated for 20–40 min and quickly immersed in an ice bath. After centrifuging, the penicillin-containing broth was replaced by the same volume of 0.9% NaCl. Another viable count was done to determine the extent to which penicillin had killed the normal population. A second set of implants on *SM* plates was then made, exactly as before. All the plates were incubated at 37° C.

With this organism, at the *SM* concentration used here, dependent (*D*) colonies appear on the plates with a characteristic delay of 1–4 days. Of thousands of *D* colonies observed in numerous experiments, none has ever been macroscopically visible 24 hr after implantation. Nondependent, resistant (*R*) colonies, on the other hand, almost always are present at 24 hr,

TABLE 1

STREPTOMYCIN-RESISTANT AND STREPTOMYCIN-DEPENDENT COLONIES APPEARING ON STREPTOMYCIN PLATES IMPLANTED WITH ALIQUOTS OF A NORMAL *E. coli* CULTURE, BEFORE AND AFTER EXPOSURE TO PENICILLIN*

SM plate	Days after implantation					Total
	1	2	3	4	5	
Before penicillin						
1	2 *R*	11 *D*	5 *D*	3 *D*	None	2 *R*, 19 *D*
2	3 *R*	7 *D*	10 *D*	2 *D*	"	3 *R*, 19 *D*
3	5 *R*	5 *D*	7 *D*	1 *D*	"	5 *R*, 13 *D*
4	4 *R*	12 *D*	11 *D*	1 *D*	"	4 *R*, 24 *D*
5	6 *R*	2 *R*, 11 *D*	6 *D*	2 *D*	2 *D*	8 *R*, 21 *D*
6	2 *R*	8 *D*	6 *D*	None	None	2 *R*, 14 *D*
Total	22 *R*	2 *R*, 54 *D*	45 *D*	9 *D*	2 *D*	24 *R*, 110 *D*
After penicillin†						
7	None	None	1 *D*	None	None	1 *D*
8	"	"	2 *D*	"	"	2 *D*
9	"	1 *D*	3 *D*	"	"	4 *D*
10	"	1 *D*	1 *D*	"	"	2 *D*
11	"	2 *D*	2 *D*	"	"	4 *D*
12	"	3 *D*	1 *D*	"	"	4 *D*
Total	None	7 *D*	10 *D*	None	None	0 *R*, 17 *D*

* Broth culture of *E. coli*: Difco nutrient broth with 0.2% glucose, inoculated with 600 cells, all sensitive to *SM*. Experiment run after 16¾ hr growth, in the phase of growth deceleration. Implants onto streptomycin plates (10 μg *SM*/ml): onto each plate 0.3 ml containing, before penicillin, 1.59×10^8 viable cells. Same implant volume was used after exposure to penicillin. Exposure to penicillin: 300 u/ml for 40 min at 37° C in fresh nutrient broth with 0.2% glucose.

† Viable after exposure to penicillin, as percentage of initial viable count, 0.120%; dependent colonies after exposure to penicillin, as percentage of initial number, 15.4%; probability that this result is due to chance—i.e., random sampling error with no differential killing by penicillin—$P \leqslant 0.001$.

although occasionally not until the following day. (The unusual lag in the initial growth of *D* colonies was first observed by Yegian, Budd, and Vanderlinde (*4*) with *Mycobacterium tuberculosis*.) When the delayed *D* colonies are subcultured on *SM* agar, discrete colonies usually grow without delay, in 24 hr. Further studies of the lag phenomenon will be reported elsewhere.

All plates were therefore incubated for 5 days, after which time no new colonies have ever been observed to appear. To avoid any possibility of accidental seeding of secondary colonies, plates were marked daily but not opened until the fifth day. At that time every colony was tested for ability to grow on nutrient agar, with and without *SM*. Heavy growth was always obtained on *SM* agar. Classification as *R* or *D* was made on the basis of growth on agar without *SM*.

The results of a typical experiment are shown in Table 1. An actively growing culture in the phase of growth deceleration was used. The mean generation time, measured during the final hour of growth, was 3.0 hr. The data presented in Table 1 show unequivocally that the bactericidal action of penicillin differentiates between normal and *D* cells. Whereas only 0.120% of the whole population survived exposure to penicillin, the corresponding figure for *D* cells was 15.4%. Thus, after penicillin, 128 times as many *D* colonies appeared as would be expected on the basis of the total viable count. If the precursors of *D* colonies were as sensitive to the bactericidal effect of penicillin as is the rest of the population, the mean expected number of *D* colonies after penicillin should be 0.120% of the number present before penicillin, or 0.132 colonies. From the Poisson distribution it can be calculated that in 87.6% of similar experiments no *D* colonies should remain after penicillin but in 11.6% a single *D* colony should be found. The probability of the observed result (17 colonies) having occurred as a result of random sampling without differential killing by penicillin is infinitesimal (less than once in 10^{29} such experiments).

In other experiments the relative killing of normal and *D* cells varied, partly as a function of the growth phase of the culture used, and partly in response to other factors not yet analyzed. In a culture that had practically ceased growth in the early stationary phase, the number of *D* colonies after penicillin was 94% of that present initially, and 37% of the whole population survived exposure to penicillin. When a culture was left in contact with penicillin for longer than 3 hr (as in the routine isolation of biochemical mutants), the entire population was practically sterilized, and no *D* cells survived. The immunity of *D* cells to the bactericidal action of penicillin is thus not absolute, but they are evidently killed more slowly than the rest of the population. This is consistent with the finding of Schaeffer (*5*) and with the author's observations that *D* cells are capable of a limited amount of slow growth in the absence of *SM*.

The complete elimination of the *R* colonies shown in Table 1 was to be expected, but no general infer-

ence can be drawn because of the small number initially present. In numerous other experiments, however, where killing by penicillin was less extreme, the number found after exposure to penicillin was reduced to about the same extent as the total viable count. This is reasonable in view of the equivalent growth rates of normal and *R* cells in nutrient broth.

The disproportionate survival of *D* variants when the total viable count is reduced by penicillin could conceivably be an artifact if for any reason the number of *D* colonies appearing in implants from a given culture was not proportional to the number of viable cells in the implants, when no penicillin had been used. Peculiar effects of this kind were noted by Barer (*6*). To rule out such a possibility, control experiments were performed in which diluted (1 : 20) and undiluted implants from the same culture were plated onto *SM* agar. The number of *D* (and *R*) colonies from the diluted implants was consistently about 5% of the number from undiluted implants. This shows that when no differential bactericidal effect is operative, the number of *D* colonies obtained from a given culture is approximately proportional to the viable count of the implant.

To show that the original small inoculum used contained no cells capable of growth on *SM*, several implants of more than 300,000 cells were made on *SM* agar. As these yielded no growth whatever, it can be confidently stated ($P < 0.002$) that the inoculum of 600 cells in the experiment of Table 1 contained no *R* or *D* cells, and that both these variants must have arisen during growth of the broth culture.

The findings reported here provide clear-cut evidence that a normal bacterial population is inhomogeneous from the standpoint of the ability to give rise to *SM*-dependent colonies on implantation onto *SM* agar. The number of *D* colonies appearing is approximately proportional to the total viable count of the implant under normal conditions, *but not when the culture has been exposed to penicillin.* After such exposure the number of *D* colonies decreases much less than the total viable count. The simplest and most satisfactory explanation of the inhomogeneity, consistent with what is known about the preferential action of penicillin upon actively growing cells, is that *SM*-dependent organisms are themselves present in a normal population before contact with *SM*. Such cells may be presumed to arise by spontaneous mutation, and may be thought of as lethal mutants which will only survive and multiply if transferred to a *SM*-containing medium. Their relative insensitivity to penicillin would result from their poor growth in the absence of the specific growth requirement, and the position would be analogous to that of the various biochemically deficient mutants. The only alternative explanation would be that precursors of *D* cells are present in a normal population, that these are relatively insensitive to penicillin, and that they only give rise to *SM*-dependent clones by some adaptive process after transfer to a *SM* medium. If slow growth were especially favorable to adaptation, the *D* precursors might be those cells in the normal population that grow most slowly and are therefore also relatively insensitive to penicillin. Experiments now in progress are designed to distinguish between these two alternatives.

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Manuscript received January 8, 1952.

Cocontraction and Reciprocal Innervation in Voluntary Movement in Man

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The coordination of muscular activity in voluntary movement involves a number of neuromuscular phenomena, one of the most important of which is the alternate action of antagonistic muscles. It has been a seemingly empirical observation known to many that antagonists cease to function when agonist muscles begin to contract. A simple example of this is the relationship of the triceps and the biceps in alternate flexion and extension of the elbow. When the elbow is flexed, the triceps is relatively inactive; when the elbow is extended, the biceps is quiet. There is no doubting the observation. However, there has been a gross oversimplification of the nature of its causation and its actual occurrence under all conditions of muscular contraction.

The most commonly accepted thesis in regard to the interrelationship of antagonistic muscles states that the contraction of a muscle produces by proprioceptive action a central inhibitory effect on its antagonist muscle. This hypothesis is based on the huge body of excellent work reported by Sherrington (*1*) in a series of classic papers. The inhibitory effect upon the skeletal muscles is not brought about through specific inhibitory nerves such as the vagus when it causes cardiac inhibition or the sympathetic nerves which cause inhibition of contraction of the intestinal muscles. Direct stimulation of motor nerves to the skeletal muscles results only in excitation. The inhibitory process is, therefore, considered to be central in origin. Stimulation of proprioceptive end organs in the contracting muscle is thought to cause cessation or diminution of excitatory impulses along the motoneuron to the antagonist muscle.

The alternate inhibition and stimulation of contraction in antagonistic muscles was labeled by Sherrington as reciprocal innervation. Innumerable experiments performed by him and by later observers substantiated the existence of this phenomenon. However, most of the observations were made with decerebrate or spinal animals or animals under anesthesia, in all

of which voluntary control was eliminated. There was a minimum of observations on actual voluntary movement. Sherrington did, however, perform a few indecisive experiments with this in mind; for example:

> I have watched with interest in Macacus the voluntary movements of the eyes after section of the 3rd and 4th nerves. In the early hours after the section, if, for instance, these nerves have been cut on the left side only, the gaze is readily directed to the left but not so readily to the right. There arises, of course, considerable external squint of the left eye. Neither when the right is directed toward the right nor when it is converged upon a light or other object just in front of the face is there more than a mere trace of movement of the left eye. Twenty-four or forty-eight hours later, when the right eye is turned to right, the left eye does perform the conjugate movement, but imperfectly and also more variably than under experimental excitation of the frontal cortex.

The close relation of the innumerable observations made under the special conditions of animal experimentation without voluntary control are not applicable without qualification to voluntary movement, especially in man. As a matter of fact, Sherrington himself pointed out that antagonists may be in contraction concurrently. This he attributed to *double* reciprocal innervation, "in which the balance between inhibition and excitation is such as to allow both half-centers to discharge, although unequally." He believed inhibition to be not only a suppressor of reflexes but a "delicate adjustor of the intensity of reflex contraction." Here again the emphasis is on reflex rather than voluntary contraction, and Sherrington himself would probably decry the oversimplification of the phenomenon as stated in a current text on physical medicine (*2*): "Reciprocal innervation means that when a voluntary or reflex contraction occurs, as in the biceps muscle, it is accompanied by relaxation of its antagonist, the triceps muscle."

Actually, as early as 1925 Tilney and Pike (*3*), in a comprehensive study, concluded that under normal conditions they were unable to observe Sherrington's phenomenon. Rather, they concluded, "muscular coordination depends primarily on the synchronous cocontractive relation in the antagonist muscle groups." Wachholder (*4*) demonstrated cocontraction in the human in a very interesting experiment. By alternately flexing and extending the elbow, he showed that when the alternate movements were performed "loosely" there was apparently no potential generated by the antagonist, but as the movements were "stiffened," cocontraction of the antagonist increased. He concluded that "reciprocal innervation of the antagonist and voluntary motion are therefore reconcilable." Actually, participation of the antagonist in the performance of it must be pointed out again that inactivity of the antagonists is not synonymous with inhibition. The apparent contradiction between Sherrington's findings in the reflex state and the observations of Tilney and Pike may be resolved if we take into account the influence of volition as a modifier of the reflex state. Observations which are true for the reflex no longer hold when volition is introduced; there is a tremendous body of work to back up such an assertion.

Our own interest in the rehabilitation of patients with neuromuscular disease has necessitated the clarification of this question. The understanding of the role of cocontraction and/or reciprocal innervation is essential not only for understanding the dynamics of normal voluntary motion in man, but also for the understanding and treatment of paralysis associated with neuromuscular disease.

Muscular antagonism must be looked upon as a relative phenomenon. Only muscles acting on single joints can be assumed to be true antagonists. Muscles acting on more than one joint may at times act as antagonists and at other times as synergists. The rectus femoris is the antagonist of the hamstring muscles at the knee, but it also helps flex the hip, so by simultaneously flexing the hip and the knee we may observe that the rectus femoris now is acting synergistically with the hamstrings. Furthermore, some muscles which functionally are considered as homogeneous are actually anatomically not so; and as a result, depending on the particular movement, one part of the muscle may act as an antagonist and another part as a synergist. The triceps is such a muscle. It has three points of origin; the lateral and medial heads arise from the humerus, whereas the long head arises from the scapula. In spite of its multiple origins, the triceps is usually listed as an extensor of the elbow joint. It does act in this capacity when the elbow is extended; however, the long head also produces extension and adduction at the shoulder, and cocontraction may occur between the biceps and the long head of the triceps if the shoulder is extended or adducted during flexion of the elbow.

Even in pure single joint antagonism, the inhibition of the antagonist is a relative matter which depends primarily on the number of motor units involved in the contraction of the agonist. In unresisted voluntary movement, there is no doubt but that the antagonist is inactive while the agonist is in contraction, but, as resistance to agonist contraction is applied, the antag-

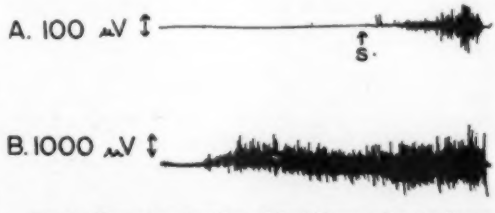

FIG. 1. Effect of contraction of the biceps on the simultaneous contraction of the triceps. The elbow is extended against maximal resistance; surface electrodes on the triceps account for tracing *B*. During this extension, at point *S*, the forearm is supinated while a recording from the biceps is made to give tracing *A*. An Offner Electromyograph with pen recorder was employed. Results indicate that during volitional extension of the elbow, the intensity of contraction of the triceps is not decreased by simultaneous supination of the forearm in which the antagonistic biceps plays a major role. The voltage gain has been adjusted so that voltages below 20 μv are not recorded.

onist begins to respond in cocontraction. The contraction of the agonist is far greater in degree than that of the antagonist, but cocontraction does occur.

As a matter of fact, the biceps and triceps will only act as antagonists if flexion or extension of the elbow is the only movement involved. If, on the other hand, the forearm is supinated during extension, full cocontraction between the biceps and the triceps occurs routinely. Furthermore, if the forearm is supinated, there is no appreciable inhibition of potential observed in the triceps when maximum resistance is applied to extension of the elbow (Fig. 1).

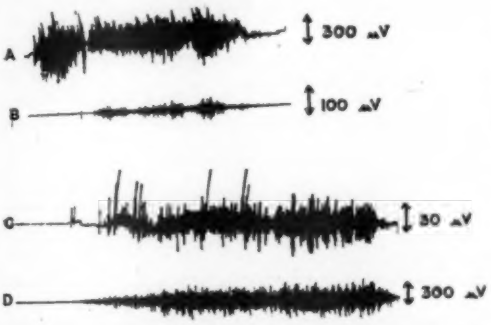

FIG. 2. Cocontraction of the antagonist muscles at the ankle during unimpeded plantar-flexion and dorsiflexion. *A*, potential obtained from the lateral head of the gastrocnemius during plantar-flexion beginning in the neutral position for the ankle; *B*, potential obtained from the anterior tibial muscle simultaneous with that recorded in *A*; *C*, potential obtained from the lateral head of the gastrocnemius during dorsiflexion of the ankle beginning in neutral position; *D*, potential obtained from the anterior tibial muscle simultaneous with that in *C*. Potential is recorded in tracing *B* simultaneously with the onset of contraction in *A*, but because of voltage gain setting, the initial low voltages in *B* are not evident in the tracing.

One type of cocontraction which has been generally neglected is the type which occurs in all antagonistic muscles in the shortened range of agonist contraction. As the agonist goes into the final range of contraction, it begins to cause proprioceptive stimulation through stretch reflexes of the antagonist muscles. The resulting contraction of the antagonist then offers resistance to the final phase of movement of the agonist, so that we have in the final movement phase of contraction a dynamic interrelationship between the contraction of the agonist and the antagonist. At the point at which the antagonist begins to contract, as a result of the proprioceptive stimulation, the agonist shows an increase in response as a result of the opposing pull of the antagonist. Quantitatively, the angle at which this phenomenon presents itself will vary with the joint and the muscles involved. In the biceps this occurs at an angle of flexion greater than 90° (the exact angle will vary with the individual), whereas at the ankle (Fig. 2) it begins to occur almost immediately and builds up to a maximum at a point in the range of flexion corresponding to the limit of the range of passive motion. The explanation for the variation between the ankle and the elbow lies in the fact that, in the elbow, the passive range of motion is very much greater than it is in the ankle. In the ankle any motion at all begins almost immediately to involve the antagonist, so that cocontraction becomes the rule in practically all motions involving the ankle.

Whereas it has been difficult to demonstrate reciprocal innervation in voluntary movement, one would expect that such would not be the case in reflex activity. Sherrington utilized the knee jerk for this demonstration. There is one condition under which we have been able uniformly to demonstrate reciprocal innervation in the human, and that is in spasticity. Many patients with neuromuscular disease evidence exaggerated activity of the spinal stretch reflex which manifests itself clinically as an increased tendency toward muscle contraction, especially during passive manipulation. This is defined as spasticity, and eventually this condition, if uncorrected, leads to contracture, a structural shortening of the muscles involved. Spasticity interferes with the full utilization of any voluntary power which the muscles may retain after paralysis and also limits the range of motion possible through movement of the joint. It thus becomes an important problem in the rehabilitation of patients with neuromuscular disease. Our own thinking has compared some forms of spasticity to decerebrate rigidity as first described by Sherrington. In this we concur with the hypothesis of Magoun and his co-workers (*5*). It was on the basis of this reasoning that we felt that reciprocal innervation should apply to spasticity in the same way that Sherrington was able to demonstrate so clearly for decerebrate rigidity. We, therefore, stimulated electrically muscles antagonistic to those exhibiting spasticity and found that relaxation of the spastic muscles could be demonstrated easily. Faradic current applied to the motor point with sufficient intensity to give a maximum contraction of the antagonist was employed. The current was applied for periods of 1 min or longer. Relaxation at times occurred instantly and at other times occurred after a short delay. Sherrington used electrical excitation of motor nerves (*1*) in animals to obtain this same form of relaxation in the demonstration of reciprocal innervation.

The relaxation was utilized to bring the affected limb through its whole range of motion. As a result, not only was relaxation evident during the application of electrical stimulation, but a persistence of the relaxation was evident in some cases for days following stimulation. With the release of the affected muscle from spasticity, techniques of neuromuscular re-education described previously (*6*) were employed to facilitate the development of latent power to its maximum. Such muscle power, which would permit the patient to carry the limb or the affected part through the full range of motion, would minimize the possibilities of a further increase in spasticity. Spasticity could also be relieved in varying degrees in those paralyzed patients where residual muscle power was not sufficiently great to bring about the restoration of voluntary movement. In such cases relaxation

of the spasticity through electrical stimulation of the antagonists permitted the passive movement of the limb through a greater range and in this way helped minimize the recurrence of the spasticity, thereby cutting down the possibilities of contracture. Details of the procedure will be described elsewhere (*7*).

We may summarize our observation by stating that in normal voluntary movement in man there is at present insufficient evidence that reciprocal innervation plays the role in the coordination of the contraction of antagonist muscles which is assumed for it by most thinking on kinesiology. Cocontraction seems to be the rule rather than the exception. On the other hand, we were able to demonstrate reciprocal innervation in patients with neuromuscular disease who showed evidence of spasticity.

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Manuscript received March 3, 1952.

Systematic Status of the Pure Culture Ciliate known as *"Tetrahymena geleii"* and *"Glaucoma piriformis"*

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Since Lwoff's (*1*) success in establishing a small holotrichous ciliate in axenic culture (i.e., free from other microorganisms), at least 50 identical or closely related members of the *Colpidium-Glaucoma-Leucophrys-Tetrahymena* group have been so grown. Some 30 of these organisms are still being maintained in various laboratories and have been used in over 250 investigations, principally of a physiological or biochemical nature, within the past 15 years (*2, 3*). The increasing importance of the experimental animals has made highly advisable a comparative morphological study in order to establish their probable taxonomical interrelationships. Twenty-six of the pure culture strains have been investigated, employing, in particular, the method of silver impregnation, an invaluable technique in study of such small and relatively undifferentiated ciliates. The present report is concerned chiefly with the 21 strains which I consider to be members of a single species but which, to date, have been carried in the literature under several different names, the most common two in recent years being *Tetrahymena geleii* Furgason, 1940, in America and *Glaucoma piriformis*[2] (Ehrenberg, 1830) Maupas, 1883, in Europe.[3] The history of these strains has been traced (*2*).

All the strains studied fall within the limits of the following brief characterization of this very widely distributed species:

Body typically pyriform in shape, 26–92 μ in length, average size about 50 μ × 30 μ; 17–22 ciliary meridians, usually 19–20, consisting of well-defined primary and secondary portions; generally 2 postoral kineties, unipolar meridians with anterior ends terminating directly at posterior margin of cytostome. Delicate apical loop at morphological apex of body; preoral suture single or double fibril from loop to cytostome; 3 intermeridional connectives, anterior end of body, roughly concentric about apical loop. Cytostome pyriform, 9–11 μ in length, about 5 μ from anterior end of body, oriented directly in body axis; characteristic tetrahymenal buccal ciliature consisting of right-hand undulating membrane and left-hand adoral zone of 3 membranelles, bases of the latter oriented at an angle of about 45° to axis of cytostome. Two to three permanent contractile vacuole pores, diameter 1 μ or less, typically located near posterior end of body in meridians 5 and 6; cytoproct slitlike in posterior end of stomatogenetic meridian 1. Macronucleus ovoid to irregularly spherical, generally not greater than 11 μ in any diameter, centrally located or slightly posterior, exhibiting typical chromatin extrusion during fission; micronucleus often absent (see below). Conjugation never observed; cysts reported by one worker (*4*).

In a study of the micronuclear problem presented by this species I have employed the Feulgen technique in critical observation of ciliates, both from axenic strains and from a number of more recently isolated bacterized strains. To date, I have examined 13 pure culture strains, using organisms from 18–20-hr cultures (rich in dividing forms) and 5–7-day cultures, and I have found all of them to be amicronucleate. The axenic strains in question were originally isolated in France, England, and in four widely separated geographical areas in the United States. Three of the American strains had been reported to be amicronucleate (*5*). Five strains, more recently isolated from various localities around Paris, and grown only in bacterized cultures, are also without micronucleus. In addition, in more than 6 cases in which the species has been found as a facultative parasite in the body cavity of living chironomid larvae (*Chironomus plumosus*), it is entirely amicronucleate.[4] A coprophilic

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[2] The trivial name was originally spelled "pyriformis" but has been written with an "i," in particular by French protozoologists, for the past 30 years.

[3] Very recently the French investigators Fauré-Fremiet and Lwoff, in several separate publications (cited by Corliss [*2*]; most recent being Lwoff's footnote, p. 325, in Kidder and Dewey [*3*]), have employed the name *Leucophrys piriformis* in reference to a number of the strains. Both these workers are now in agreement with the writer that the species should be called *Tetrahymena pyriformis* (personal communications).

[4] I have also isolated a second, very closely related, species of *Tetrahymena* from *Chironomus*, sometimes from the same larvae. It is frequently found in conjugation and is very likely the ciliate reported once before (*6*). Its micronucleus is prominent, generally 2.5–3.0 μ in diameter. Full description will be published later.

ciliate kindly supplied by C. A. Hoare, of London—the strain described as *"Glaucoma piriformis"* (*4*)—also shows no evidence of a micronucleus. One may, perhaps, justifiably conclude that the amicronucleate condition in this species is of widespread and common occurrence. On the other hand, one investigator (*7*), also employing the Feulgen technique, has recorded the presence of a micronucleus in members of an extinct strain of this species. Also, I have observed it in preparations (belonging to E. Fauré-Fremiet) of a second bacterized strain from the Paris region, likewise no longer being maintained, in which it is typically in a depression of, or embedded in, the macronucleus. Its size is small (under 2 μ), but it can be clearly differentiated from rounded-up masses of chromatin extruded from the macronucleus during fission. At the present time, therefore, one should hesitate to assume that the American strains of *"Tetrahymena geleii"* being cultured axenically are amicronucleate until all of them have been subjected to careful examination.

In agreement with Furgason (*5*), I consider the ciliate a member of the genus *Tetrahymena* Furgason, 1940, but I have suggested (*8*) that *Tetrahymena* is the same genus as that to which Ehrenberg (*9, 10*) invalidly applied the name *"Leucophrys."* I further consider the ciliate as probably specifically identical with Ehrenberg's *"Leucophrys pyriformis."* His descriptions and figures of the organism leave something to be desired in the matter of fineness of detail, but there is nothing in them which cannot be reconciled with Maupas' (*11*) redescription of this species and with the characterization offered above. That Ehrenberg's figures show 9–11 ciliary striations on one surface, and that he never observed the occurrence of conjugation, also support—or at least do not contradict—the identity of the forms. Maupas erred in transferring the ciliate to the genus *Glaucoma,* but in his detailed description of *"G. pyriformis"* there again appear to be no characteristics given which contravene those found by Furgason (*5*) for *"T. geleii"* or by the writer for a large number of strains belonging to the same species. It is true that Maupas misinterpreted the relationships among the cytostomal organelles, very difficult to resolve without modern techniques, but he recognized their similarity to those in the closely related ciliate *"Leucophrys patula"* (*12*).

By application of the Law of Priority (Art. 25, *International Rules of Zoological Nomenclature*) all more recent names applied to the organism under consideration may be regarded as subjective synonyms of the first proposed name, keeping in mind the alleged nonavailability of the generic name *"Leucophrys"* for these particular ciliates and the suggested conclusion that *"Tetrahymena"* is chronologically the next available published name (*8*). Lwoff (*13*), without description, figures, or discussion, and spelling the trivial name with an "i," used the combination considered correct by the writer and therefore the full name would become *Tetrahymena pyriformis* (Ehrbg., 1830) Lwoff, 1947. It is the type species of the genus. Lwoff's ciliate, strain GL, cultured axenically without interruption for 30 years, may be considered as the type strain of the species.

In a longer publication a more detailed description of this species will be offered, with attention to minor variations among the various strains. Also, the relationship of *T. pyriformis* to some 5 or 6 congeneric species[5] which have been, or are now being, investigated by the writer, including in particular *T. vorax* (Kidder, Lilly, and Claff, 1940) Kidder, 1941 and *T. patula* (Müller, 1786) Corliss, 1951, will be discussed. That the 3 extant axenic strains of *T. vorax,* PP, V_1, and V_2 (only the last of which appears still capable of undergoing profound transformations in its life cycle), have all been found to be amicronucleate presents a problem of some interest regarding the phylogenetic relationship between this species and *T. pyriformis.*

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Manuscript received February 18, 1952.

[5] Since this paper was submitted for publication, I have received from A. M. Elliott, University of Michigan, pure culture strains of the very interesting ciliate, species not yet determined, whose cytogenetics has been investigated by Elliott and Nanney (*Science,* **116**, 33 [1952]). Preliminary morphological study indicates that although the organism is similar in many respects to members of the axenic strains of *T. pyriformis,* it possesses certain characteristics which appear to differentiate it slightly from that species as the latter has been described in the present paper.

Differential Stability of Various Analogs of Cobalamin to Vitamin C

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The conversion of vitamin B_{12} (cyanocobalamin) to vitamin B_{12b} (hydroxycobalamin) through the sulfite was reported in 1949 from this laboratory (*1*). The discovery was made independently in two laboratories that vitamin B_{12b} (B_{12a}) is destroyed quickly by ascorbate, whereas vitamin B_{12} is destroyed relatively slowly (*2, 3*). Coordination of the cobalamin ion with various anions has been described (*4–6*), and these findings illuminate our early observation on the stabilizing effect of sulfite (*2*). The ascorbate reaction

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FIG. 1. Stability of vitamins B_{12} and B_{12b} at varying pH heated 3 hr at 98°–99° C.

was first used as a means of differentiating vitamin B_{12} and B_{12b} in high-potency concentrates, but was soon found to be unreliable for relatively crude preparations. The purpose of this paper is to describe experiments with known cobalamin analogs, and to point out certain of the limitations of the reaction as an analytical tool.

Vitamin B_{12b} isolated from fermentation sources (*1*) was used in early studies of the reaction with vitamin C. Advantage was later taken of the method of converting vitamin B_{12} to vitamin B_{12b} by photolysis (*5*).

Solutions of crystalline vitamins B_{12} and B_{12b}, 20 μg/ml, were made up in one-tenth standard concentration McIlvaine buffers. The pH range studied was from 2.6 to 8.0. The tightly stoppered solutions were subjected to streaming steam for 1 hr in the autoclave, cooled promptly, and assayed microbiologically. It was clear from this study (Fig. 1) and others that vitamin B_{12} is generally more stable than vitamin B_{12b}.

A standard method for the differential assay with ascorbate was worked out with known mixtures of crystalline vitamins B_{12} and B_{12b} in aqueous solution. To 2 ml of test solution, containing 20–40 μg of vitamin B_{12}, is added 80 mg of a 1:4 ascorbic acid: sodium ascorbate mixture. The pH of the solution is then 4.5–5, and no buffer is required. The solution is heated for ½ hr at 65° C, cooled promptly, and placed on microbiological assay. Under these conditions, destruction of vitamin B_{12b} is 95% or more, and of vitamin B_{12} about 5%.

Tests run on a number of commercial vitamin B_{12} concentrates revealed that many of them contained predominantly vitamin B_{12b}. Some of these concentrates were pure enough so that it was possible to check the results of the differential ascorbate method by spectrophotometric assay. The characteristic absorption spectra maxima at 3510 A for vitamin B_{12b} and at 3610 A for B_{12} was used in calculating the concentration of each form of the vitamin. There was close agreement between the two methods.

Application of the ascorbate method to liver extracts and to crude fermentation concentrates did not prove satisfactory. None of the naturally occurring amino acids, purines, pyrimidines, and metabolites tested had significant protective effect. However, as little as 10 mg of liver extract solids largely prevented the destruction of 40 μg of vitamin B_{12b} by 80 mg of ascorbic acid–sodium ascorbate mixture. Although purified liver extracts differ in their protective ability, crude liver extracts were uniformly effective. The protective property was found to reside in the ash, chiefly in the iron and copper. Iron salts are particularly effective, having demonstrable effect at .001% concentration of iron. Catalysis of the oxidative destruction of ascorbate by iron is well known, but any bearing this may have on the present phenomena is not clear.

Of the common anions tested, only sulfite, nitrite, and cyanide proved effective in stabilizing vitamin B_{12b} to ascorbate. Complete protection against ascorbate in aqueous solution is achieved in presence of approximately 100 molecular equivalents of sulfite or nitrite. At least 10 molecular equivalents of either are needed before significant protection to ascorbate occurs. Similar amounts of sulfite and nitrite are needed before the characteristic changes in spectra become apparent. This is in contrast to cyanide, where only 1 molecular equivalent is needed at pH 7 to convert vitamin B_{12b} to cyanocobalamin, as evidenced both by the shift in absorption maxima and stability to ascorbate. The effect of graded additions of materials which showed significant protection is shown in Table 1. Although thiocyanate (*7*), histidine (*8*), and ammonia (*8*) are reported to form complexes with vitamin B_{12b}, excesses of these materials did not protect vitamin B_{12b} from destruction by ascorbate.[2] An intrinsic factor concentrate of duodenum, 100:1 (Viobin), had no protective effect in a ratio of 1 mg concentrate/μg of vitamin B_{12b}.

TABLE 1

INFLUENCE OF SOME ADDITIONS ON STABILITY OF VITAMIN B_{12b} TO ASCORBATE

Addition to vitamin B_{12b}, 30 μg/ml	Activity remaining after ascorbate treatment (% of original)
None	0–4
KCN, 0.5 mol equiv*	38
" 1.0 " "	93
$NaHSO_3$, 1 mol equiv	8
" 10 " "	20
" 100 " "	94
$NaNO_2$, 1 mol equiv	2
" 10 " "	42
" 100 " "	96
$FeCl_3 \cdot 6H_2O$, .005%	7
" .02%	40
" .1%	86

* Molecular weight of cobalamin estimated as 1400.

[2] It is of interest that an excess of ferro- or ferricyanide was protective, whereas thiocyanate or cyanate appeared to have no effect.

The rapid and nearly complete disappearance of color in the reaction with ascorbate indicates release of cobalt from cobalamin. Cooley *et al.* (*8*) offer the hypothesis that, in the case of cyanocobalamin, cyanide acts to strengthen the bond between the cobalt and benziminazole nitrogens, thus making for greater stability than is the case for hydroxycobalamin. Unusual resonance energy is imputed to the cobalt-cyanide complex, giving a positive charge to the cobalt atom and thereby strengthening the Co—N bond.

The following procedure was used to test whether cobalt is liberated in the cobalamin-ascorbate reaction. Ten mg of crystalline vitamin B_{12} was dissolved in 5 ml water. The pH was made to 3.5 with dilute HCl, and the solution was irradiated 4 hr. Conversion from the cyano form was spectrophotometrically complete. To this solution was added 100 mg of the ascorbate mixture, with immediate color change from red to brown. This reaction mixture was designated solution X. Less than 1% of the original vitamin activity remained in solution X by microbiological and rat assays.

The nitroso R salt method for cobalt determination was set up, using $CoCl_2 \cdot 6H_2O$ as a standard. Test solution X gave a characteristic color with nitroso R salt, which was read in the spectrophotometer at 5100 A. About 80% of the theoretical cobalt reacted with the reagent as measured colorimetrically against either a water blank or solution X blank. Vitamin B_{12b} in comparable concentrations of cobalt completely obscured any color resulting from addition of nitroso R salt.

In order to determine whether the cobalt of solution X was in free or combined form, extraction was carried out with CCl_4-dithizone reagent according to the standard method (*9*) for separation of cobalt. The extract, after ashing, gave a characteristic color test for cobalt. Recovery of the cobalt of the original vitamin B_{12b} was 80%. The CCl_4-dithizone solution, on the other hand, failed to extract a measurable amount of cobalt from a solution of crystalline vitamin B_{12b}. These results suggest that ascorbate actually releases cobalt from the vitamin B_{12b} molecule.

Sodium thioglycollate, cysteine hydrochloride, and thiomalic acid, in 1–4% concentration in water, all destroy vitamin B_{12b} more rapidly than they destroy vitamin B_{12}. The difference in rate or extent of destruction of the two forms of the vitamin is not, however, nearly as marked for these materials as for ascorbate. Of the reducing compounds tested, only thiosorbitol approached ascorbate in speed and completeness of destruction of vitamin B_{12b}. Thiosorbitol, like ascorbate, has much slower destructive effect for vitamin B_{12}. Sulfite also protects against destruction by these sulfhydryl compounds.

These studies indicate that the susceptibility of cobalamin to degradation by vitamin C is a function of the coordination of its key cobalt atom with various anions. Only those anions which coordinate strongly with cobalt appear capable of protection. Differentiation between strongly and weakly coordinated forms of the vitamin by reaction with ascorbate is useful and reliable, but only for highly purified concentrates free from iron and other interferences.

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Manuscript received March 3, 1952.

The Metabolism of Betaine and Sodium Formate by Leukemic Mice[1]

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In a previous report it was shown that leukemic mice excrete increased quantities of creatine and allantoin (*1*). It was suggested that this increased creatine excretion reflected an increased rate of synthesis of creatine which was associated with the rapid rate of leucocyte production. It seemed desirable to obtain direct evidence that the increased creatine excretion of leukemic mice reflects an accelerated rate of synthesis and is not merely the result of loss of body stores of creatine. We have consistently been unable to obtain creatine synthesis *in vitro* by incubation of mouse liver preparations with the precursors of creatine. In order to measure the rate of creatine synthesis we have injected control and leukemic mice with C^{14}-labeled sodium formate and C^{14} methyl–labeled betaine and determined the excretion of labeled creatine in a subsequent 24-hr period. In addition, the excretion of C^{14}-labeled allantoin has also been determined. The results support the hypothesis that the elevated excretion of creatine by leukemic mice is the result of an increased rate of synthesis.

The animals were mice of the DBA strain, and leukemia was induced as previously described (*1*). Leukemic mice were taken 10 days after blood transfer; the controls were mice of the same strain which had not been inoculated with leukemic blood. Six control and 6 leukemic mice were each injected with 90 μg (4 μc/μM) of sodium formate and placed in metab-

[1] Research paper No. 973, Journal Series, University of Arkansas. This work was supported by a grant-in-aid from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

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TABLE 1

THE EXCRETION OF LABELED CREATININE AND ALLANTOIN BY CONTROL AND LEUKEMIC MICE IN A 24-HOUR PERIOD AFTER INJECTION OF C^{14}-LABELED SODIUM FORMATE AND C^{14} METHYL-LABELED BETAINE

Substance injected	Total counts injected	Animals	Total creatinine		Allantoin	
			Counts/ min/mouse	Counts/ min/μM	Counts/ min/mouse	Counts/ min/μM
Sodium formate	1×10^8	Control	317	54	1190	80
" "	1×10^8	Leukemic	796	115	2900	142
Betaine	4.7×10^8	Control	656	94	416	20
"	4.7×10^8	Leukemic	913	92	706	21

olism cages. Pooled 24-hr urine samples were collected from each group. For the betaine experiments 10 control and 10 leukemic mice were each injected with 1 mg of betaine hydrobromide (0.53 μc/μM), and urine collections made as in the formate experiments. The urine was autoclaved with acid to convert creatine to creatinine. The creatinine was isolated by carrier isolation and purified as the zinc chloride derivative. Allantoin was isolated by carrier isolation. The total creatinine and allantoin content of the urine before carrier addition was determined in order that specific activity could be determined. The samples were placed on aluminum plates and counted with an end window tube with a window thickness of 2 mg/cm².

In addition to the carrier isolation, the urine samples were subjected to paper chromatography in a phenol water system. The specific activities of creatinine and allantoin as determined by counting the paper strips agreed quite well with the results obtained by carrier isolation procedures.

The results presented in Table 1 show that the leukemic mice excreted more labeled creatinine and allantoin after injection of labeled sodium formate or betaine than did the controls. There is adequate evidence that animals can synthesize methyl groups from one-carbon precursors (*2*), and the relative specific activities of the creatinine and allantoin excreted by these mice after labeled formate injection indicates that the mouse is able to utilize formate quite effectively as a precursor of creatine. The results also indicate that betaine may be used effectively as a precursor of allantoin. The conversion of methyl to a one-carbon fragment which can serve as a precursor of the β-carbon of serine (*3*), and which may be incorporated into purines (*4*), has been demonstrated. Betaine was more effective as a creatine precursor than as a precursor of allantoin. This is in agreement with the observations that the methyl group may be transferred *in toto* (*5*).

The fact that the leukemic mice excreted more labeled creatinine after sodium formate or betaine injection is proof that at least a part of the increased creatine excretion by leukemic mice is the result of an accelerated rate of creatine synthesis (*1*). These results in conjunction with other findings indicate that creatine (*1, 6*) and methyl groups (*7–9*) must play a significant role in white blood cell formation.

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Manuscript received February 15, 1952.

Effect of Excess Dietary DL-Methionine on Liver and Kidney Catalase of Rats[1]

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In a preliminary investigation upon the effect of single amino acids on catalase activity, we have noted an effect of excess DL-methionine on liver and kidney catalase activity. Protein-free diets containing concentrations of 3–5% of glycine, L-cystine, arginine, leucine, tryptophan, and asparagine were without effect on the catalase activity of protein-depleted rats. DL-methionine produced a marked depression of kidney and liver catalase activity, and further data were obtained with this amino acid.

Adult female Wistar rats were placed on a protein-free diet for 2 weeks and then placed on the diets indicated in Table 1. All diets were administered *ad lib.* The protein-free diet and catalase assay method have been described previously (*1*). The toxic effect of 5% DL-methionine at 10% gelatin concentration is prevented by increased levels of dietary protein. This is in accord with previous observations wherein increasing dietary protein reversed the toxicity displayed by methionine toward growth (*2*) and nitrogen balance (*3*).

The depression and elevation of kidney catalase activity with changes in the concentration of dietary

[1] This work was supported by a grant from the University of California cancer research funds.

TABLE 1

METHIONINE EFFECTS ON LIVER AND KIDNEY CATALASE ACTIVITY

Diet after 2 weeks protein-free diet	No. days on diet	Liver catalase activity*	Kidney catalase activity*	Kidney wt (%)
10% Gelatin, 5% methionine	2	222	23	0.73
" " " "	4	173	19	0.87
" " " "	9	87	9	0.95
25% " 1% "	9	418	68	0.80
25% " 3% "	9	276	47	0.78
25% " 5% "	9	386	29	0.83
25% Casein, 5% "	9	485	12	1.07
Control rats on normal diet	—	550 ± 50	36 ± 4	0.72 ± .04
" " " protein-free diet	—	265 ± 30	39 ± 5	0.68 ± .04

* Catalase unit = ml of O_2/sec/100 g body wt from 1 *N* hydrogen peroxide at 0° C.

methionine and protein suggest that there are different effects of methionine toxicity upon the liver and kidney. The present data and previous observations on the effect of excess dietary protein in increasing kidney catalase activity (*4*) indicate that catalase may be involved in some aspect of protein metabolism.

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Manuscript received March 6, 1952.

Comments and Communications

Inactivation of Circulin by Lipase[1]

PETERSON and Reineke showed (*J. Biol. Chem.*, **181**, 95 [1949]) that circulin, a mixture of basic peptides produced by *Bacillus circulans* Q19, loses its antibiotic activity against *Escherichia coli* ATCC 26 when incubated with a lipase preparation that was free of proteolytic activity as tested by the Mett method (F. C. Koch. *Practical Methods of Biochemistry* [1934]). This observation prompted them to suggest that 6-methyloctanoic acid, which circulin is thought to contain in addition to L-threonine, D-Leucine, and L-α, γ-diaminobutyric acid (DABA), is joined to the peptide through threonine by an ester linkage. To avoid premature acceptance of such a view, we wish to stress the fact that some of the assumptions on the basis of which the existence of this linkage was suggested have not yet been proved. For example, Peterson and Reineke believed circulin to be a *cyclic* polypeptide, taking the following into consideration: (1) amino acid composition (threonine, leucine, and DABA seem to be present in a ratio of 1:1:5); (2) the fact that approximately one half of its amino nitrogen is uncombined (the amino nitrogen before hydrolysis was 7.5%; after hydrolysis, 15.8%); (3) the absence of free carboxyl groups, as shown by titration curves and a negative ninhydrin-CO_2 (Van Slyke) test; and (4) evidence that the amino groups of DABA were the only free amino groups in circulin. The fourth line of evidence is subject to some question and is being reinvestigated. It was based on the observation that the 2,4-dinitrophenyl (DNP) derivative of circulin, when hydrolyzed with HCl, apparently yielded no other products than DABA, α-amino-γ-(2,4-dinitroanilino)-butyric acid, threonine, and leucine, as observed by paper chromatography. However, since DNP derivatives of mono-amino acids do not react with ninhydrin, which was used to indicate the position of the various components on the chromatogram, and are visible only because of their yellow color, small quantities of such derivatives may have escaped detection. Moreover, the fact that not all the DABA appeared as its DNP derivative in the chromatogram makes one wonder whether (1) DABA is formed from its DNP derivative by acid hydrolysis, (2) the dinitrophenylation was not carried to completion, or (3) some DABA is combined in the intact molecule. The first hypothesis can be experimentally disproved (R. G. Shepherd, personal communication) and can therefore be excluded as an explanation for the occurrence of free DABA on the chromatogram. The second alternative is not unlikely, inasmuch as the dinitrophenylation was performed in the absence of alcohol, a condition under which the reaction is thought not to go to completion. This, however, does not exclude the third possibility, especially since the data on the combining weight of circulin were inconsistent. If circulin has a combining weight of approximately 300, as claimed, and actually has five free amino groups, its molecular weight should be 1500. However, calculations from the weight of the constituents that circulin is thought to contain indicate a molecular weight

[1] We are grateful to R. G. Shepherd, of the American Cyanamid Company, Stamford, Conn., for his stimulating comments on this problem.

close to 900. Accordingly, it would seem that either the determinations for the combining weight were inaccurate, or fewer than five amino groups are free.

Although it is possible that circulin has a cyclic structure, the contentions that all its free amino groups are furnished by DABA, and that all DABA side chains are unsubstituted, still remain to be proved. This proof is prerequisite to the claim that an O-acyl, rather than an N-acyl, linkage exists between 6-methyloctanoic acid and the rest of the molecule. Moreover, one needs to demonstrate that the lipase preparation used does not hydrolyze N-acyl, as well as O-acyl, linkages. Isolation of the fatty acid and the intact peptide after inactivation of circulin by lipase, and demonstration that a hydroxyl group rather than an amino group becomes liberated during inactivation, are also necessary before any concept on the manner in which the fatty acid is attached to the rest of the molecule can be accepted.

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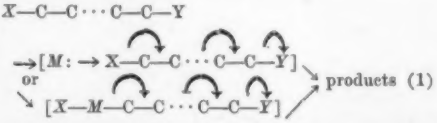
The Action of Metals on 1,4-Dihalides and Similar Compounds

A STUDY is under way to determine the extent and mechanism of the general reaction



M is a metal such as magnesium, zinc, or sodium (other reducing agents, such as iodide ion, may also function in the reaction); *X* is halogen; and *Y* is an electronegative group—e.g., halogen. The dotted line represents a multiple bond.

Earlier examples of Equation (1) include the reaction of zinc or magnesium with 1,4-dibromo-2-butenes to yield 1,3-butadienes (*1, 2*), and the reaction of γ-phenoxycrotyl bromide with magnesium to yield 1,3-butadiene (*1*). More recently, the authors reported the formation of butatriene in high yield from 1,4-dibromobutyne-2 and zinc in diethylene glycol diethyl ether (*3*). With zinc in ethanol or water, butatriene was formed in only small yield, the principal product being butadiene. An extensive study of the properties of unsubstituted cumulenes such as butatriene has been undertaken.

Other examples of the general reaction (*1*) have now been found. Thus, magnesium in tetrahydrofuran reacted with γ-bromocrotonaldehyde diethylacetal to yield 1-ethoxy-1,3-butadiene in 78% yield, and with γ-bromocrotonaldehyde diacetate to yield 1-acetoxy-1,3-butadiene in 60% yield. Ethyl ortho-γ-bromocrotonate and magnesium yielded a material which largely polymerized in the tetrahydrofuran solvent. Treatment of the reaction mixture with hot aqueous HCl gave a small yield of crotonic acid. This could have resulted from the expected product of the reaction with magnesium, 1,1-diethoxy-1,3-butadiene, by reaction of this ketene acetal with water to yield ethyl crotonate (or ethyl vinylacetate) and then hydrolysis to the acid.

Iodide ion perhaps can be substituted for the metal in the above elimination reactions. For example, potassium iodide in aqueous methanol converted 1,4-dibromo-butene-2 to butadiene-1,3, and 3,6-dibromocyclohexene to cyclohexadiene-1,3. That some degree of unsaturation in the carbon chain is required is shown by the fact that 1,4-dibromobutane failed to yield any ethylene when treated with magnesium.

Other examples on which the elimination reaction (1) will be tried include γ-chlorocrotonylchloride, γ-chloropropiolic acid chloride, fumaryl and maleic acid chloride, and acetylenedicarboxylic acid chloride. Perhaps the reaction also can be extended to six carbon analogs, such as the conversion of 1,6-dibromohexadiyne-2,4 to hexapentaene.

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Three- and Four-Dimensional Plotting

THE examination of experimental results by plotting a graph in two dimensions is almost universal, but little use is made of plots of variables in three dimensions. The lack of a suitable simple apparatus for plotting in three dimensions is one reason for the neglect of this potentially useful technique. In connection with a statistical analysis of data on acid, chloride, and volume for samples of gastric juice (R. B. Fisher and J. N. Hunt. *J. Physiol.*, **111**, 138 [1950]), a simple method of plotting in three, and even four, dimensions was worked out, and it may be of value to other workers with similar problems.

The apparatus shown in Fig. 1 consists of a cube of Lucite constructed of 20 numbered sheets of the same thickness locked together by two bolts and illuminated from below by a small electric bulb. The lowest sheet is ruled with a grid. To plot in 4 dimensions, two dimensions are represented by the position of points plotted in waterproof ink on the surface of the plates, the third dimension is represented by the number of the plate selected, and the fourth by the color of the ink used to plot the point. In practice,

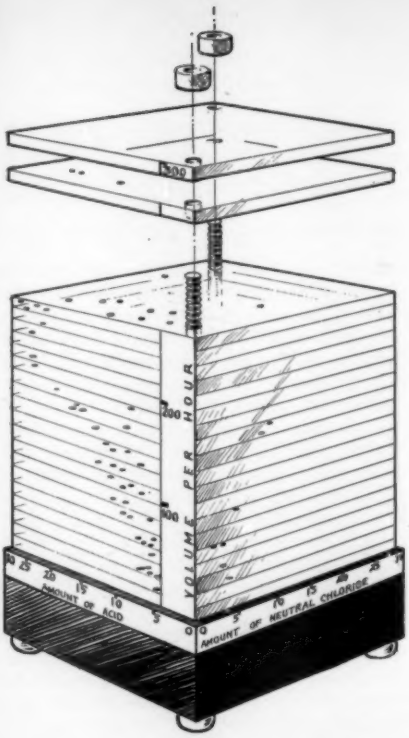

FIG. 1.

the data, previously classified, can be put into the block quickly and cleaned out again with alcohol when it is no longer required.

Inspection of data through the top face of the block allows a quick appreciation of the relationship between and among the variables and may suggest the type of statistical analysis to be used. The block also has value in demonstrating the meaning of three- and four-dimensional regression equations to those without formal statistical training.

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Unscientific Reporting

THE problem of getting accurate information to the public is frequently complicated by the changes and distortions of the newspapers. The following case history is an example.

In a telephone interview with a reporter of the Baltimore *Sun*, I stated that there are about as many cats as rats in Baltimore and, among other things, that cats eat few rats during a year. When the story appeared in the February 22, 1952, issue of the *Morning Sun* the headline read: SCIENTIST BLAMES LAZY CATS FOR CITY'S LAG IN RAT RACE. The story was picked up by other papers, and I received abusive letters or cards accusing me of being unfair to the rat-catching abilities of our feline friends. The latest (probably not the last) version appeared in the *New York Times Magazine* (April 6, 1952), as follows: "Dr. David E. Davis, Johns Hopkins School of Hygiene and Public Health: 'Baltimore cats are just plain lazy. If the cats would catch just one rat each, the city's rat problem would be solved'." Note that quotation marks were used around a reporter's version of a headline writer's version of a reporter's version of what I said over the telephone!

Fortunately in this case the distortion caused no bad consequences and did no harm. But how can accurate information be transmitted to the public without distortion? This amusing case history is trivial, but the problem of accuracy in transmisison must be solved.

DAVID E. DAVIS

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UPON reading the article "Reporting Science," by Frank Carey, in your April 18 issue, it occurred to me that at least three news items that appeared rather recently in the press as if they were very new indeed could have been "cut down to size" by the addition of background information easily obtained by a few telephone calls to local scientists.

The article in which the use of synthetic resins as a substitute for distillation in the purification of water should have included the information that the discovery, which was the subject of the item, was merely an improvement on rather old fundamental work.

The article on a new cancer cure (zinc chloride) would have been more enlightening had the information been added that the AMA listed this cure in the cancer section of *Nostrums and Quackery* at least thirty years ago.

The big news about seeding clouds with dry ice to initiate precipitation should have included the information that three airplanes had in 1930, in Holland, seeded clouds with solid carbon dioxide for the same purpose, and that the results at that time were said to be promising.

Supplementary material of this nature would have improved the articles or ruined them, depending upon the point of view.

NORRIS M. ERB

Riviera Beach, Maryland

CONCERNING Baltimore's cats and rats, if the doctor was misquoted as he says, then there's NO excuse. It was just poor reporting by a man who would probably do a poor job on any kind of a story, science or otherwise.

I have no doubt that such things occur every now and then—and I made no claim in my article that every science story in the news is always accurate. I did point out that the men who are doing science day

in and day out on the news run bend over backward to make their stories accurate. And that would be true, also, of the *good* nonscience reporter. Newspapers, especially really good ones like the Baltimore *Sun*, have ways of finding out the inaccurate man.

As to the *New York Times Magazine* allegedly manufacturing or synthesizing quotes . . . well, there's NO excuse for that, either, but I'll bet the *Times* would raise the devil with the reporter if they knew about it!

As for background material, the first question that arises is: How much information was given by the sources of these stories—presumably scientists themselves? The scientist has the first obligation to include all data pertinent to the report he is making, and if he intentionally leaves out any historic background that might be important, his is the primary blame. If a reporter gets a story from a man with a good scientific reputation, he would naturally assume that he was getting the truth as the scientist saw it. Of course, if it were an obviously controversial subject, a good reporter would seek comment from possible dissenters. If a story emanates from questionable sources, the reporter has a distinct obligation to check on it. If he doesn't, he shouldn't be in the business.

Next question: On the "zinc chloride" story, did your correspondent or the AMA take the trouble to write in to papers pointing out that the "cure" had been listed in *Nostrums and Quackery*? It seems to me that he should have done so—and that papers would have been glad to print what he said on its news merits.

FRANK CAREY

Associated Press
Washington, D. C.

Periodic Acid-Schiff Reaction of the Insect Cuticle

HOTCHKISS (*1*) described the use of periodic acid as a histochemical reagent. It has the property of reacting with the α-glycol (—CHOH—CHOH—) group, rupturing the bond between the two carbon atoms, and converting the two alcoholic groups to aldehydic groups. Insoluble compounds containing the α-glycol group can be located in tissue sections by the use of periodic acid followed by Schiff's reagent, which gives a colored reaction product with the aldehyde that is produced.

Hotchkiss supposed that the majority of periodic acid-Schiff (PAS) positive substances that are likely to be present in tissues would be polysaccharides. Richards (*2*), on applying the test to the insect procuticle, found that the result was not always positive and postulated that the chitin, being a polysaccharide, must be "masked." The chitobiose units, which constitute chitin, however, are substituted in such a way as

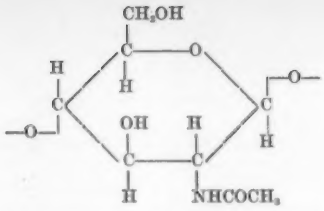

FIG. 1. Structural unit of chitin (after Meyer [*3*]).

to contain no α-glycol group (Fig. 1), and there is therefore no reason to suppose that chitin should give a positive PAS reaction (*4*). "Purified chitin" (i.e., cuticle after treatment with hot 10% NaOH solution) does give a positive reaction (*2*), because the alkali deacetylates the chitobioses. Since the PAS test was first introduced, it has been shown that a positive reaction is also given by the α-amino-β-hydroxy (—CHOH—CHNH$_2$—) group (*5*), so that whether or not the amino group (as well as the acetal-group) is removed from the chitin by alkali treatment, it could be expected to give a positive result in the PAS test.

To say that polysaccharides are present in tissue which is PAS-positive is not necessarily a valid conclusion. Having obtained a positive reaction with the epicuticle of a number of insects, Richards (*2*) has claimed that polysaccharides are present there, in the face of much biochemical evidence to the contrary; but it has been shown that the cells of the right colleterial gland of *Periplaneta*, which produces the phenolic substance that tans the ootheca, contain polysaccharide-free granules that are PAS-positive (*6*). From Pryor's work (*7*), it is reasonable to infer that substances similar to those found in the right colleterial gland are likely to be found also in the hardened regions of insect cuticle; and if one makes this inference, the more reasonable conclusion is reached that it is the phenolic cuticular tan, and not a hypothetical polysaccharide, which gives the positive PAS reaction in the epicuticle.

Lillie (*8*) has shown that the contents of the cells of the mammalian adrenal medulla are phenolic and are PAS-positive; the same situation prevails in the colleterial gland and is described elsewhere in detail (*6*).

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Book Reviews

The Merck Index of Chemicals and Drugs. 6th ed. Rahway, N. J.: Merck & Co., Inc., 1952. 1167 pp. $7.50; thumb-indexed, $8.00.

Our children's great-grandfather was not long out of medical school when the first edition of the *Merck Index* appeared in 1889. Any book that has weathered the changes in medicine and chemistry that have taken place since then deserves real scrutiny. The original purpose and design must have been sound indeed. As stated in an earlier preface, they were that the book should be "a condensed, comprehensive and reliable Encyclopedia of Chemicals and Drugs for the chemist, pharmacist, physician and those in allied professions." The book remains just that, even though the growth of chemistry surely has swelled it beyond the original authors' most expansive dreams.

One thousand of the 1100-odd pages are filled with an alphabetical listing of chemicals, some 8000 in all, with a brief statement of structure, physical characteristics, and use. It is thus more than a dictionary and is, in fact, a concise encyclopedia. Also, as is obvious from the number of entries, it is not only a collection from medicinal chemistry, but from other fields as well. Inorganic, as well as organic, compounds are considered. One might say that this portion of the book differs from the *Handbook of Chemistry and Physics* and the Eastman catalogue in being larger and more annotated, and from the multivolumed Heilbron's *Dictionary of Chemical Compounds* in being more compressed and medicinal. For the average worker in biology and medicine this compromise is exactly right and probably has had much to do with the long life of the book.

Therapeutic credulity has stiffened in the past 63 years, and it is pleasing to see that the statements of medical usefulness of previous volumes have been deleted right and left. In this respect, the *Index* should not be confused with the smaller *Merck Manual,* in which a good deal of credulity is still visible.

The remaining sections of the book are mostly in an appendix containing some 30 useful lists or tables, which run from organic "name" reactions to the Greek alphabet and four-place logarithms. Once one has learned what these sections are, they become useful indeed. The usual error is in not realizing that they exist, and it will pay the new user to look them over attentively.

In a sense, it is a pity that this volume differs from some of the previous editions, in that the authors remain anonymous, for it would be nice to know to whom one's thanks for such a classic should be directed.

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Tensor Analysis: Theory and Applications. I. S. Sokolnikoff. New York: Wiley; London: Chapman & Hall, 1951. 335 pp. $6.00.

This book appears exactly half a century after the publication of the first extensive report on the tensor calculus by its creators, G. Ricci and T. Levi-Civita. The theory of relativity produced a rash of enthusiasts for the new calculus. But there were many, even among the greatest mathematicians, who were temperamentally not inclined to become adepts of the art of indices. Today, most scientists have adopted a more dispassionate view on tensors and will welcome the appearance of another excellent book on the subject.

The book consists of six chapters: "Linear Vector Spaces," "Tensor Theory," "Geometry," "Analytical Mechanics," "Relativistic Mechanics," and "Mechanics of Continuous Media."

As one might expect from an author of many successful textbooks, the presentation is well balanced and makes pleasant reading. An interesting feature is a formulation of the essential ideas of nonlinear mechanics of continuous media in the most general tensor form.

Some details in the exposition may be evaluated differently by various readers, but it seems certain that *Tensor Analysis* will take its rightful place among the standard texts.

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University of Maryland

The Oxide-Coated Cathode, Vol. 1: ***Manufacture***; Vol. 2: ***Physics, Including Thermal Emission from Metals and Semi-Conductors.*** G. Herrmann and Phil S. Wagener; trans. from the German by Phil S. Wagener. London: Chapman & Hall, 1951. Vol. 1: 148 pp., 21s; Vol. 2: 311 pp., 42s.

The authors have given in two volumes of moderate size a well-organized presentation of a subject on which a large amount of work has been done. The first volume deals with the techniques of manufacture, their effects on the properties of the cathode, and the methods of measuring different characteristics of the cathode. Such information is useful not only for those primarily interested in production but also for those doing research in this field. The second volume presents the physics of thermionic emission. The first section gives a concise but clear treatment of emission current from metals and from metals with adsorbed films of foreign material. A discussion of ionic solids and energy bands in semiconductors is then presented in sufficient detail for an understanding of the nature of oxide-coated cathodes and their emission properties as discussed in the remainder of the book. The derivations of the equations are clear and easily understood.

These two books are up to date and cover most

phases of the subject. Although their size limits detailed discussion of specific points, the essential features are treated adequately. There are numerous tables and graphs giving various representative data. Comprehensive lists of references, one following each chapter, will also be found useful.

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Department of Physics, Purdue University

Hevea: Thirty Years of Research in the Far East. M. J. Dijkman. Coral Gables, Fla.: Univ. Miami Press; Waltham, Mass.: Chronica Botanica, 1951. 329 pp. $6.00.

The natural rubber industry is founded on *Hevea brasiliensis,* which with all its close relatives, is native to the Amazon Valley. The tree has come into significance in the twentieth century as a cultivated plant. Early developments, until halted by World War II, were especially great in Indonesia. A fungus that causes a devastating leaf blight has held American plantings in check, but under forest conditions the fungus does not build up a great enough concentration of spores to be serious. Fortunately, the disease has not been introduced to other parts of the world.

In times of crisis, the United States has invested heavily in the exploitation of wild rubber of various kinds and has also spent money freely for rubber research. The past decade has witnessed such expenditure, and a fair share has gone to *Hevea* investigations. Prior to 1941 the great majority of studies on *Hevea* as a cultivated plant were carried on in the Far East. Many of the most important publications are accordingly written in Dutch.

Dr. Dijkman is Dutch—born in Java, educated in The Netherlands, and with wide rubber experience in Java. He is now assistant professor of tropical botany at the University of Miami. He attempts in this book to summarize the literature on rubber in the Far East and to relate to it publications from other areas that are pertinent. The chief value of his work is that he overcomes for us the barrier of language and has seemingly reviewed in accurate manner the *Hevea* reports in Dutch. That service is highly useful. But evidently he himself occasionally stumbles over language barriers: in at least one instance he has confused the contributions of two different American writers—he repeatedly refers to Adolpho Ducke, the Brazilian botanist who has published extensively on *Hevea,* as "Duke."

The book has 17 chapters devoted to the whole range of topics relating to the cultivation of *Hevea,* with references at the end of each chapter. Included are 116 figures, 93 tables, and 5 appendices giving data on rubber exports by countries, acreages in rubber, comparative yields for clones, characteristics of certain clones, a glossary, etc. The volume has one index for authors, another for subjects, and is an excellent source of specific information.

J. T. Baldwin, Jr.

Department of Biology
College of William and Mary

Scientific Book Register

Principles of Mathematical Logic. D. Hilbert and W. Ackermann; trans. from the German by Lewis M. Hammond, George G. Leckie, and F. Steinhardt; Robert E. Luce, Ed. New York: Chelsea Pub., 1950. 172 pp. $3.50.

Dynamic Aspects of Biochemistry. 2nd ed. Ernest Baldwin. New York: Cambridge Univ. Press, 1952. 544 pp. $5.00.

Eiweiss ('Albumin.') Heinrich Hellmann. Stuttgart, Germany: Curt E. Schwab, 1952. 163 pp. 5.80 DM.

Electronic Analog Computers (D-C Analog Computers). Granino A. Korn and Theresa M. Korn. New York–London: McGraw-Hill, 1952. 378 pp. $7.00.

Management Controls in Industrial Research Organizations. Robert N. Anthony, with assistance of John S. Day. Boston, Mass.: Division of Research, Harvard Business School, 1952. 537 pp. $6.75.

The Counter-Revolution of Science: Studies on the Abuse of Reason. F. A. Hayek. Glencoe, Ill: Free Press, 1952. 255 pp. $4.00.

Methods of Algebraic Geometry, Vol. II; Book III: General Theory of Algebraic Varieties in Projective Space; Book IV: Quadrics and Grassmann Varieties. W. V. D. Hodge and D. Pedoe. New York: Cambridge Univ. Press, 1952. 394 pp. $7.50.

The Human Pelvis. Carl C. Francis. St. Louis: Mosby, 1952. 210 pp. $5.00.

Handbook of Engineering Fundamentals. 2nd ed. Ovid W. Eshbach, Ed. New York: Wiley; London: Chapman & Hall, 1952. 14 sections. $10.00.

Annual Review of Medicine, Vol. 3. Windsor C. Cutting, Ed., and Henry W. Newman, Assoc. Ed. Stanford, Calif.: Annual Reviews, 1952. 442 pp. $6.00.

Thermodynamics and Statistical Mechanics. William P. Allis and Melvin A. Herlin. New York–London: McGraw-Hill, 1952. 239 pp. $6.00.

The Auger Effect and Other Radiationless Transitions. E. H. S. Burhop. New York: Cambridge Univ. Press, 1952. 188 pp. $5.50.

Automatic and Manual Control. Papers contributed to the Conference at Cranfield, England, 1951. A. Tustin, Ed. New York: Academic Press; London: Butterworths, 1952. 584 pp. $10.00.

A Course in College Chemistry. V. R. Damerell. New York: Macmillan, 1952. 587 pp. $5.50.

Foundations of Analysis: The Arithmetic of Whole, Rational, Irrational and Complex Numbers. A Supplement to Text-Books on the Differential and Integral Calculus. Edmund Landau; trans. from the German by F. Steinhardt. New York: Chelsea Pub., 1951. 134 pp. $3.25.

The Origin of Life and the Evolution of Living Things: An Environmental Theory. Olan R. Hyndman. New York: Philosophical Library, 1952. 648 pp. $8.75.

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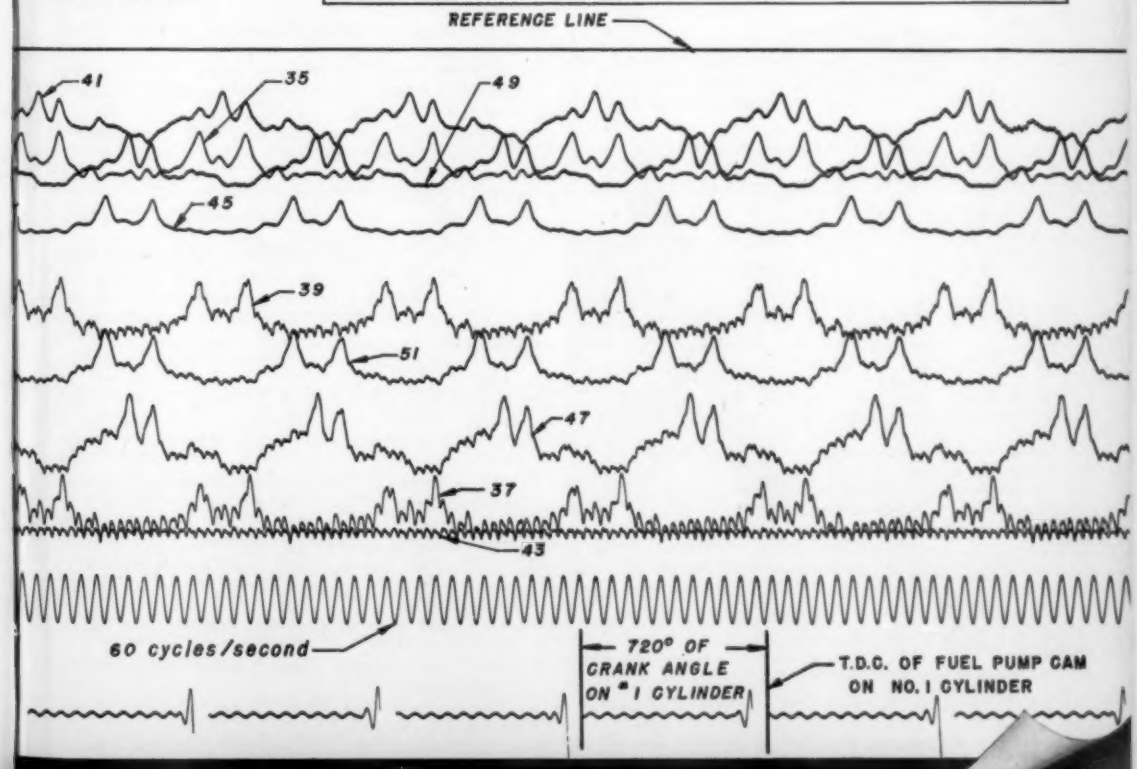

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Meetings & Conferences

Aug. 11–21. Union Radio-Scientifique Internationale. Sydney, Australia.
Aug. 12–15. Poultry Science Association. University of Connecticut, Storrs.
Aug. 12–16. Photographic Society of America (Annual). Hotel New Yorker, New York.
Aug. 12–16. Plant Science Seminar (Annual). Philadelphia.
Aug. 15–22. International Conference of Agricultural Economists. East Lansing, Mich.
Aug. 17–23. American Pharmaceutical Association. Hotel Bellevue-Stratford, Philadelphia.
Aug. 17–23. International Grassland Congress. Pennsylvania State College, State College.
Aug. 18–22. Seminar in Industrial Instrumentation. Minneapolis-Honeywell Regulator Company, Philadelphia.
Aug. 19–22. American Institute of Electrical Engineers (Pacific General). Hotel Westward Ho, Phoenix, Ariz.
Aug. 20–27. Australian and New Zealand Association for the Advancement of Science (Annual). Sydney.
Aug. 20–28. International Congress on Theoretical and Applied Mechanics. Istanbul.
Aug. 22–30. Australasian Medical Congress. Melbourne.
Aug. 24–27. International Union against Tuberculosis. Rio de Janeiro.
Aug. 24–30. International Congress on Diseases of the Chest. Rio de Janeiro.
Aug. 25–29. Oak Ridge Summer Symposium on "The Role of Atomic Energy in Agricultural Research." Oak Ridge, Tenn.
Aug. 25–30. Pan-American Union of Engineering Societies. New Orleans.
Aug. 25–30. World Federation for Mental Health (Annual). Brussels.
Aug. 31–Sept 7. Interamerican Cardiological Congress. Buenos Aires.
Sept. 1–2. Mathematical Association of America, Inc. (Summer). Michigan State College, East Lansing.
Sept. 1–3. International Spectroscopy Colloquium. London.
Sept. 1–6. American Psychological Association. Washington, D. C.
Sept. 1–6. International Congress on Astronautics. Stuttgart.
Sept. 1–8. World Congress of Anthropology and Ethnology. Vienna.
Sept. 1–12. Biological Photographic Association. Hotel New Yorker, New York.
Sept. 2–5. American Mathematical Society (Summer). Michigan State College, East Lansing.
Sept. 2–5. Conference on Science, Philosophy and Religion. Columbia University, New York.
Sept. 2–5. International College of Surgeons, U. S. and Canadian chapters (Annual). Conrad Hilton Hotel, Chicago.
Sept. 2–6. Conference on Magnetism. University of Maryland, College Park.
Sept. 3–9. International Union for the Protection of Nature. Caracas.
Sept. 3–10. British Association for the Advancement of Science (Annual). Belfast.
Sept. 4–9. International Congress on Analytical Chemistry. Oxford, Eng.
Sept. 4–13. International Astronomical Union. Rome.

Longmans books

Flood & West

DICTIONARY OF SCIENTIFIC AND TECHNICAL WORDS

By W. E. Flood and Michael West. A pronouncing and explanatory dictionary, for those with little scientific knowledge, based on about fifty scientific terms, using a vocabulary of about one thousand explanatory words, covering about ten thousand items, in some fifty different fields of knowledge. 1952; ready. 397 pages, double column; line cuts. $2.25.

Chatterjee

BENGAL IN MAPS

By S. P. Chatterjee, University of Calcutta. A geographical analysis of the distribution of resources, industries and population in West Bengal and Eastern Pakistan. 1949. 105 pp. 11½ x 9 inches. 79 black and white maps; one folding black and white map. Descriptive and analytical text. $6.50.

Revesz

INTRODUCTION TO THE PSYCHOLOGY OF MUSIC

By G. Revesz, University of Amsterdam. Translated by Geraldine de Courcy. A general survey of the important problems involved in the psychology of sound and music. 272 pp. Illus. Ready, Sept. 1952. About $5.25.

McLean & Cook

TEXTBOOK OF THEORETICAL BOTANY

By R. C. McLean and W. R. Ivimey Cook, both of the University of Wales. In four volumes.

Vol. I, Cytology, plant classification, and descriptions of plants up to the Angiosperms. 1951. 1069 pp. 314 figs. 727 photographs. $13.50.
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By R. C. McLean and W. R. Ivimey Cook. A descriptive guide for laboratory work, designed to accompany the above TEXTBOOK OF THEORETICAL BOTANY; contains Ten Parts: Methods, Cytology, Evolutionary Morphology, Angiosperms, Sexual Reproduction of Angiosperms, Plant Physiology, Modification of Normal Plant Form, Plant Ecology, Variation and Heredity; and four appendices. 472 pp. 127 figs. Ready, Sept. 1952. About $7.00.

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Program content

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2. Programs of the 18 AAAS sections and subsections (symposia and contributed papers).
3. Programs of the more than 30 participating societies.
4. The Special Sessions: AAAS, Academy Conference, Conference on Scientific Manpower II, National Geographic Society, Phi Beta Kappa, RESA, Sigma Xi.
5. Details of the Kiel Auditorium, downtown hotels, Washington University.
6. Titles of the latest scientific films to be shown in the AAAS Science Theatre.
7. Exhibitors in the 1952 Annual Exposition of Science and Industry and descriptions of their exhibits.

Directory content

1. AAAS officers and staff for 1952.
2. Complete roll of AAAS presidents and their fields.
3. The 236 affiliated organizations.
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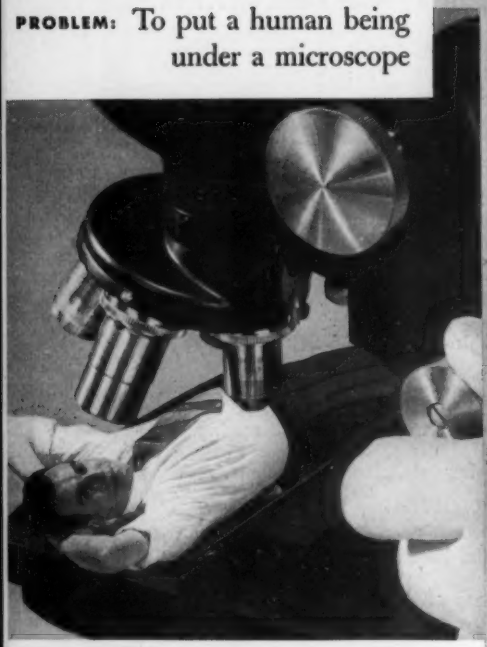

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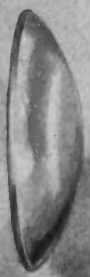

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